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FROM HEALTH FOOD STORES AND LEADING CHEMISTS

BRITISH MEDICAL JOURNAL

LONDON SATURDAY NOVEMBER 14 1953

VALVOTOMY IN THE TREATMENT OF MITRAL STENOSIS

BY

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The selection of patients who need surgical treatment for mitral stenosis is a problem which is no longer confined to special centres for cardiac surgery. If patients who are in greatest need of surgical treatment, and who are most likely to benefit from it, are to be given priority, selection must start with the practitioner and in the general medical clinic.

The advent of valvotomy as a method of treatment has stimulated an intensive investigation of the pathological physiology of mitral stenosis by means of cardiac catheterization and related technical procedures. This has led in turn to a renewed interest in the interpretation of clinical signs and symptoms. Many physical signs which have been a source of speculation since the early days of auscultation can now be more precisely interpreted in the light of surgical experience and of recent haemodynamic research. Many of the patients in the present series, and a great many others judged unsuitable for operation, have been investigated by cardiac catheterization, and, at the start, the information so obtained often fortified the decision for or against operation. But with increasing experience we are now seldom influenced by catheter findings in selecting favourable cases for surgery. Admittedly, in extending the scope of surgery to less favourable cases, full investigation is still desirable.

The low mortality and good results of mitral valvotomy are already well known, and it is with the indications for operation that we are now mainly concerned. In this respect we were guided from the start by the pioneer work at Guy's Hospital (Baker, Brock, and Campbell, 1950) and in the United States (Harken *et al.*, 1948; Bailey, 1949), but our present views have been moulded largely by personal experience.

SELECTION OF CASES FOR VALVOTOMY

Basic Indications.—The aim of surgical treatment of mitral stenosis is to remove or reduce valvular obstruction without thereby creating serious valvular incompetence. Provided the fused mitral cusps are split or cut along the line of the commissures, as advocated by Brock, the degree of incompetence need not be increased, and may even be diminished, by valvotomy. The basic indications for mitral valvotomy may therefore be simply stated as follows: (1) Severe stenosis of the mitral orifice, the anatomical conformation of which must be suitable for surgical correction. (2) The patient's symptoms must be disabling enough to warrant the risks of surgery. (3) We must be satisfied that the symptoms are entirely or mainly due to mitral obstruction, and not to myocardial or other valvular lesions, or to extracardiac causes.

Degree of Mitral Stenosis and its Anatomy

If mitral stenosis were a purely mechanical constriction of the valvular orifice, of unvarying anatomical form, and superimposed on an otherwise healthy heart, it would be a relatively simple matter to assess its degree, but in practice the problem is far more complex. We have to take account of the anatomical form of the valvular structures, of secondary changes in the lung vessels, and of complicating factors such as myocardial damage, auricular fibrillation, and associated aortic and tricuspid valve lesions. Nevertheless, in many cases the rheumatic damage falls mainly on the mitral valve cusps.

The ideal type of stenosis for surgical correction is the *diaphragmatic valve* well described by Balfour (1898) as follows: "The condition of the valve generally associated with the presystolic murmur is that usually termed a diaphragmatic valve in which the two segments of the mitral valve are united and stretched like a diaphragm across the auriculo-ventricular opening. This diaphragm, as we may call it, is thickened especially at the edges of the central opening. . . ." Apart from the thickened orifice, the mitral diaphragm as a whole may be relatively pliant, and it can be split so as to re-create mobile and supple valve flaps, and so that obstruction is relieved without incompetence resulting (Type I, Fig. 1). The diaphragmatic valve, which is formed mainly by the large antero-medial or aortic cusp, cannot open or close, but, if still pliant, it balloons like a sail towards the auricle in systole, and billows back towards the ventricle in diastole. This sudden tension of the mitral diaphragm, first in one direction and then in the other, gives rise to important physical signs, which are discussed below.

Sometimes the valve sheet as a whole is indurated and thickened so that ballooning is reduced and at the same time valvotomy made more difficult technically (Type II, Fig. 1). Most valves in this category cannot be completely divided, but an adequate result may be achieved if one commissure is split and the other only partly split. Here the extent of shortening or fibrosis of the chordae tendineae is greater than in Type I, and mobile cusps cannot be reconstructed.

More severe rheumatic damage may fuse the cusps, chordae, and papillary muscles into a rigid, fibrous, funnel-shaped structure directed towards the ventricle (Type III, Fig. 1). If cases for surgery are carefully selected, the surgeon seldom encounters this type of stenosis, which features so prominently in textbooks of pathology. Here little can be done by operation, yet digital dilatation has occasionally produced unexpected clinical improvement.

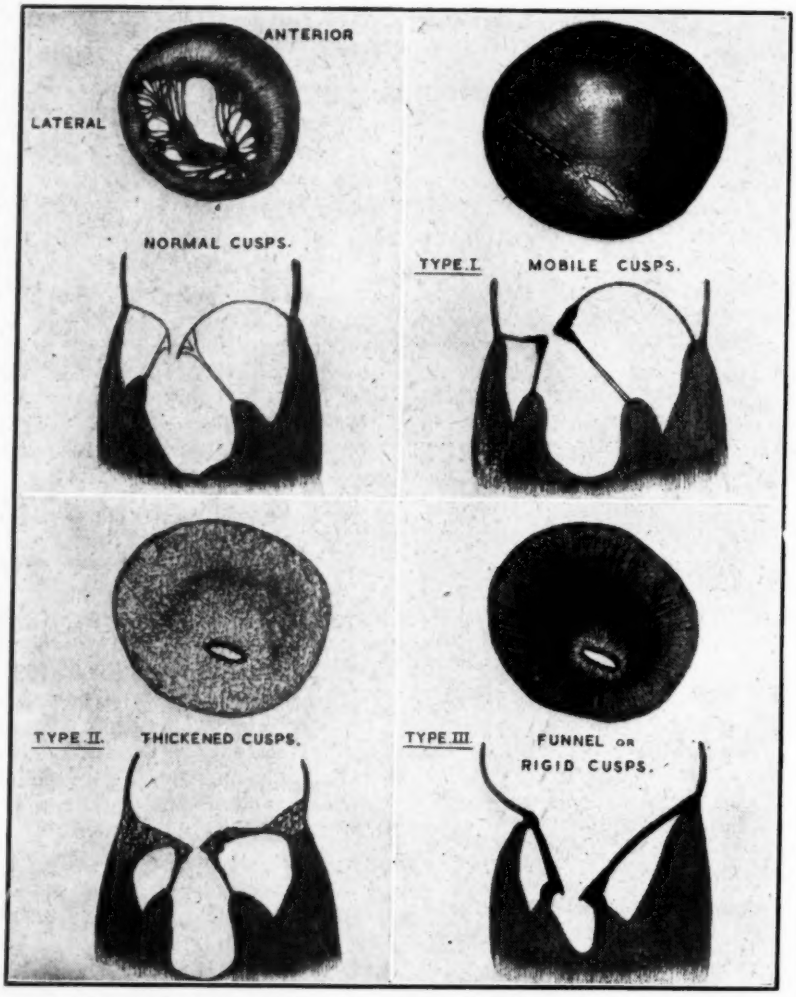

FIG. 1.—Types of mitral stenosis. The features of each type are described in the text.

Deformed and retracted cusps producing a permanently gaping and incompetent orifice, even though some degree of stenosis may be present, are not amenable to surgical reconstruction. Graham Steell (1906) and Carey Coombs (1924) regarded mitral regurgitation as due mainly to dilatation of the left ventricle and of the mitral ring from myocardial damage during the active phase of rheumatic carditis, so that subsequent fibrosis of the cusps failed to constrict the enlarged orifice appreciably. Others regarded the left ventricular enlargement as the result rather than the cause of mitral regurgitation. Whichever view is taken, and both may be correct under different circumstances, the fact remains that left ventricular enlargement and mitral incompetence go together, and both are probably incompatible with a severe degree of mitral stenosis. An enlarged left ventricle should be regarded as evidence of myocardial damage, whether of inflammatory or of mechanical causation.

Clinical Signs

The clinical signs of a *pliant diaphragmatic valve* are, first and foremost, the snapping first sound, and the characteristic apex beat described by Broadbent (1897) as "tapping," an adjective originally applied to the first sound by Sansom (1892). Carey Coombs described the apex beat of mitral stenosis as follows: "The hand placed over the praecordium feels the apex bang suddenly and sharply against the chest wall, then sink away from it as suddenly as it arrived." These signs relate to a sudden tension of the pliant mitral diaphragm as it is ballooned upwards into the auricle in systole, and can be felt by the surgeon's finger. We may well speak of this sign as the "closing snap" of the mitral valve. So long as a snapping first sound is audible, and it is best heard with the patient lying and inclined toward his left side, serious mitral incompetence and a hopelessly rigid valve are unlikely, and a systolic murmur may be ignored.

Another important sign of a diaphragmatic valve is the opening snap, a sharp click which follows closely after the second sound and which is best heard over the mesocardium often internal to or above the apex beat. The opening snap, formerly described as a double second sound at the apex, was first recognized by Sansom as originating at the mitral valve, and the term "claquement d'ouverture" is generally attributed by French writers to Potain. It may be supposed that the opening snap is caused by sudden tension of the pliant mitral diaphragm in a reversed direction to that responsible for the snapping first sound—namely, towards the ventricle at the start of diastole. We believe that a loud opening snap of clicking quality is a reliable sign of mitral stenosis with a pliant diaphragmatic valve and that it constitutes important evidence of operability. The opening snap is absent in predominant mitral regurgitation, and is uncommon or lacks a loud clicking quality in severe mitral calcification (Mounsey, 1953; Wynn, 1953).

In regard to murmurs, loud rumbling diastolic and presystolic murmurs completely filling diastole constitute reliable evidence of considerable mitral stenosis, though this does not necessarily imply an operable valve. The absence of an impressive mitral diastolic rumble does not exclude severe stenosis, and Levine and Love (1952) have drawn attention to the occasional absence of all diastolic murmurs in this condition. The intensity of the diastolic murmur depends not only on the degree of stenosis but also on the flow through the mitral orifice, and active pulmonary vasoconstriction acts as a barrier to mitral flow. In cases with

severe pulmonary hypertension the mitral diastolic murmur may be quite insignificant, though the opening snap tends to persist.

A mitral systolic murmur need not imply serious incompetence in the presence of a snapping first sound and an opening snap; it may be ignored unless there is evidence of left ventricular hypertrophy in the form of an apex beat with a localized and sustained thrust, the "choc en dôme" of Bard. If the first sound is diminished or replaced by a systolic murmur, and the left ventricle is enlarged, the case is probably unsuitable for valvotomy. The electrocardiogram and radiograph are valuable in identifying left ventricular hypertrophy. In evaluating left ventricular enlargement *vis-à-vis* the mitral valve, due regard must be given to the presence of aortic incompetence.

The pulse in severe mitral stenosis is of small volume and sustained in character, and, like the small aorta, is evidence of a restricted output from the left ventricle. It is especially small in cases with active pulmonary hypertension, when the cardiac output is further reduced by a second mechanical barrier in the lungs. In predominant mitral regurgitation the pulse has a more jerky character.

A small hypoplastic aorta is the rule in severe mitral stenosis developing before adult life, and the aortic knuckle is small in the radiograph, situated well below the clavicles, and sometimes invisible in the anterior view.

To sum up, we regard the following clinical signs of mitral stenosis as indicative of a pliant diaphragmatic valve amenable to valvotomy: a snapping apex beat; a snapping first sound (closing snap); and a loud opening snap of clicking quality. Additional evidence of severe mitral stenosis is provided by intense diastolic and presystolic murmurs; a small sustained pulse; and a small hypoplastic aorta in the radiograph.

Signs of Right Ventricular Enlargement

When the right ventricle enlarges, the infundibulum is first involved, causing a palpable systolic impulse on the left of the sternum, usually in the third interspace and well above the apex beat. A diastolic shock due to forcible closure of the pulmonary valves is also felt over the enlarged infundibulum.

The main cavity of the right ventricle enlarges towards the left, displacing the left ventricle posteriorly away from the chest wall. In pure mitral stenosis, therefore, an apex beat displaced to the left is evidence of right ventricular enlargement. The right ventricle seems to strike the chest broadside, so that the apex beat resembles a blow with the open hand, compared with a blow by the closed fist from the left ventricle, which strikes the chest head on. Instead of a localized thrust, the enlarged right ventricle causes a diffuse and less-sustained pulsation between sternum and apex beat which, in mitral stenosis, also has a snapping quality.

In radiographs, right ventricular enlargement gives the heart a square shape with blunted apex, compared with the pointed oval of left ventricular enlargement. Right heart enlargement may also be identified in the left oblique view.

Symptoms

Breathlessness is the earliest symptom in the majority of cases and its onset is usually gradual. Patients notice that they can no longer keep pace with their friends, carry their shopping, or perform their usual domestic duties without distress, and their disability is best assessed in terms of their capacity for these simple everyday tasks. Sometimes attention is first called to the heart by more dramatic symptoms of a characteristic kind.

In 1921, and more fully in 1934, Gallavardin described the occurrence of paroxysmal pulmonary oedema in certain cases of mitral stenosis, which he called "le rétrécissement mitral œdémateux," and this particular syndrome was also described by Oppenheimer and Schwartz (1933) and by McGinn and White (1934). It is encountered especially in women aged 25 to 35 years with long-standing mitral stenosis. The paroxysms of dyspnoea are often provoked by effort or emotion, but may also occur spontaneously at night, and tend to be aggravated during the menstrual period, during pregnancy, and in cold weather. Gallavardin noted that in such patients the heart was little if at all enlarged, the rhythm was regular, and digitalis was ineffective in controlling the breathlessness.

Careful interrogation is necessary to identify minor paroxysms provoked by effort; once dyspnoea attains a certain degree the following symptoms appear—oppression in the chest, severe palpitation, tracheal bubbling and wheezing, cough, and blood-stained expectoration. These symptoms subside gradually with rest. Spontaneous or nocturnal attacks tend to be more severe, may be accompanied by circulatory collapse, and may prove mortal. Sooner or later these patients become orthopnoeic, require extra pillows for sleep, and exhibit some degree of persistent pulmonary congestion. The patient with "oedematous mitral stenosis" is severely incapacitated and offers a marked contrast to the patient with a huge heart, auricular fibrillation, and congestive failure reasonably controlled by digitalis, who may lead a relatively comfortable though restricted life.

Paroxysmal pulmonary oedema is explained by a sudden increase in pulmonary capillary pressure above the level of the colloid osmotic pressure of the plasma. Opposed by severe mitral obstruction, any increase in the output of the right ventricle—for example, on exertion—must elevate the pressure in the pulmonary veins and capillaries. In the past it was difficult to explain why pulmonary oedema should occur in certain cases of severe mitral stenosis and not in others, often with far larger hearts; the probable explanation is that in some cases the pulmonary arterioles are constricted, thus limiting the output of the right ventricle and so protecting the lung capillaries from any sudden overdistension. In mitral stenosis with pulmonary oedema, pulmonary hypertension is a purely passive process, due to a rise in pressure behind the obstructed mitral valve, and the absence of cardiac enlargement and of auricular fibrillation indicates that the myocardium is relatively intact. This combination of severe mechanical obstruction and a sound myocardium represents the ideal condition for surgical intervention.

Classification of Cases for Surgical Purposes

For the purpose of deciding suitability for valvotomy and for assessing its results, a classification based purely on symptoms or the degree of incapacity is unsatisfactory. A patient with symptoms of great severity may be most eligible for surgical relief, whereas another far less troubled may be entirely beyond it.

The pulmonary arterial pressure at a given moment is not a reliable basis for deciding on surgical treatment unless it is interpreted in relation to the clinical signs and symptoms, and a complete haemodynamic investigation is not always practicable even in expert hands. We believe that, eventually, suitability for valvotomy will usually be decided on the basis of routine cardiological examination rather than on catheter findings. The primary indication for valvotomy is severe mitral obstruction with an operable valve, and in this respect the clinical signs of a pliant diaphragmatic valve are significant. Next in importance is the size of the right ventricle. If tricuspid disease is excluded, right ventricular enlargement provides the best measure of the degree of permanent damage resulting from mitral stenosis, and thus it is the best guide in regard to the prospect of surgical relief. At the Middlesex, having selected the cases with operable valves, we graded them for surgical purposes into three classes, identifiable by routine cardiological examination:—Class I: cases without or with minimal signs of right ventricular enlargement; class II: cases with con-

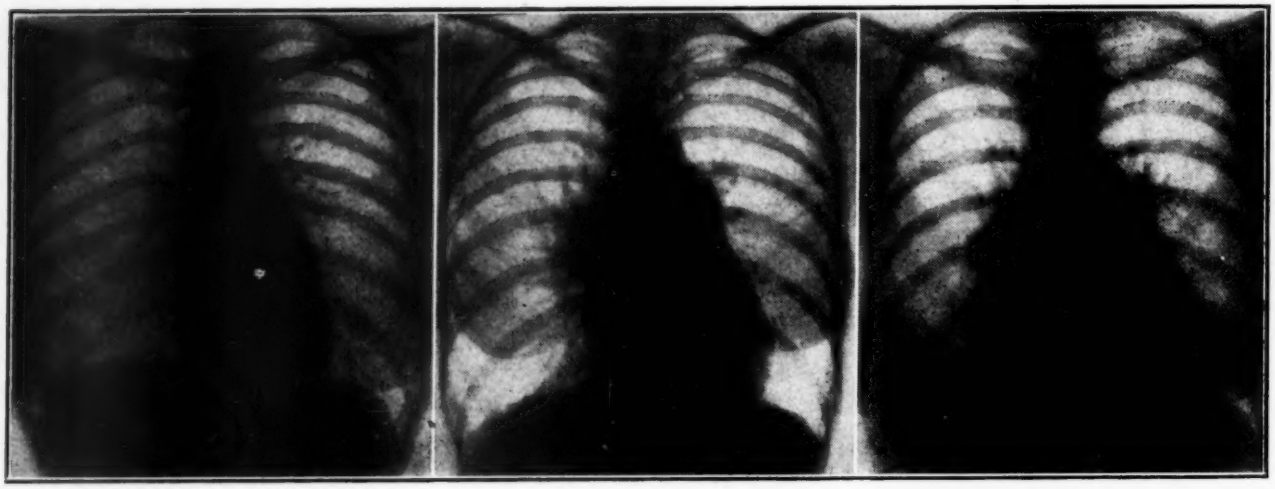

FIG. 2 FIG. 3 FIG. 4

FIG. 2.—Mitral stenosis with clinical signs of slight right ventricular enlargement (class I). The patient, a woman aged 36, in sinus rhythm, had several attacks of pulmonary oedema. Valvotomy was performed with a good symptomatic result (Case 55). FIG. 3.—Mitral stenosis with clinical and electrocardiographic evidence of right ventricular enlargement (class II). The pulmonary artery and its hilar branches were dilated. Mean pulmonary arterial pressure was 54 mm. Hg. The patient, a woman aged 28, was considerably restricted by breathlessness. A good result followed valvotomy. FIG. 4.—Mitral stenosis with considerable cardiac enlargement (class III). Cardio-thoracic ratio 68%. Mean pulmonary arterial pressure was 48 mm. Hg. The patient, a woman aged 48 with auricular fibrillation, had recurrent attacks of congestive failure which improved with treatment.

siderable right ventricular enlargement, but without congestive failure; class III: cases with gross right ventricular enlargement and congestive failure.

Class I.—Regular rhythm was more common than auricular fibrillation, the pattern of right ventricular hypertrophy was seldom present in the electrocardiogram, and radiography showed a mitral configuration without much increase in transverse diameter of the heart. There was often perihilar congestion, but without great dilatation of the pulmonary artery (Fig. 2). The mean cardio-thoracic ratio in this group was 51%. Paroxysmal pulmonary oedema was common. The mean pulmonary arterial pressure averaged 35 mm. Hg.

Class II.—Right ventricular enlargement was evident clinically, radiologically, and in the electrocardiogram. Normal rhythm was more common than auricular fibrillation, and paroxysmal pulmonary oedema was less frequent than in class I. In some cases, episodes of congestive failure occurred, due to the onset of fibrillation or to pulmonary infarction, but failure was not persistent. Dilatation of the pulmonary artery and its hilar branches was evident in radiographs, but perihilar oedema was often absent (Fig. 3). The mean cardio-thoracic ratio was 55%. The mean pulmonary arterial pressure averaged over 50 mm. Hg, indicating active pulmonary hypertension. These patients have severe mitral obstruction with some myocardial damage.

Class III.—The heart was considerably enlarged, the cardio-thoracic ratio exceeding 65% (Fig. 4). Aortic valve disease was present in some cases, and often tricuspid incompetence. Auricular fibrillation was invariable, and congestive failure was recurrent or could not be completely relieved by treatment. The liver was permanently enlarged and presumably damaged. Patients in this class posed the problem of whether the mitral obstruction played a sufficiently important part in the overall picture to justify mitral valvotomy. If the signs of a pliant diaphragmatic valve were present it was thought that some measure of surgical relief was at least possible.

Table I presents an analysis of the first 72 cases operated on at the Middlesex Hospital, classified as described.

Results

Mitral valvotomy has been performed on 150 patients—87 at the Middlesex Hospital and 63 at Harefield Hospital and the London Chest Hospital. There were 31 men and 119 women, a ratio of 1 to 4. The youngest patient was 19 and the oldest 57; 78% were between 30 and 49. The heart rhythm was regular in 88 patients (59%), and auricular fibrillation was present in the remaining 62 (41%). The incidence of certain other clinical features is mentioned below.

Four of the 150 patients operated on died as a direct result of the operation—that is, within four days—an immediate operative mortality of 2.7%. Four others died after an interval of one month or longer. Details of these fatalities are given later.

TABLE I.—*Mitral Valvotomy: Analysis of the First 72 Cases Operated on at the Middlesex Hospital. Results According to Classification*

Class	No. of Cases	Duration of Symptoms (Years)	Orthopnoea	Paroxysmal Dyspnoea	Haemoptysis	Pulsus Parvus	R.V. Pulsation	Pulmonary Diastolic Shock	Auricular Fibrillation	E.C.G. Signs of R.V. Enlargement	Pul. Arterial Pressure* (mm. Hg)	Pul. Capillary Pressure* (mm. Hg)	Cardio-thoracic Ratio (%)	Results†	
														Good	Fair or Poor
I	33	6	21 (64%)	20 (61%)	25 (76%)	9 (27%)	23 (70%)	14 (42%)	10 (31%)	0 (0%)	35	20	51	73%	23% 1 late death
II	30	7	17 (57%)	9 (30%)	20 (67%)	14 (47%)	25 (83%)	22 (73%)	6 (20%)	30 (100%)	54	25	55	69%	19% 1 operative death, 1 late death
III	9	12	8 (89%)	6 (67%)	4 (44%)	1 (11%)	5 (56%)	2 (22%)	8 (89%)	1 (11%)	28 55	19 22	63	40%	20% 2 operative deaths
Total	72		46 (64%)	35 (49%)	49 (68%)	24 (33%)	53 (74%)	38 (53%)	24 (33%)	31 (43%)					

* In class III there were two results only. † Results apply to 61 cases adequately followed up.

One hundred and eleven patients have been followed up for periods of five months to two and a half years. The results are given in Table II. The remaining 39 have been

TABLE II.—*Mitral Valvotomy: Results*

Result in 111 cases:		
Good	81	(74%)
Fair	9	(20%)
Poor	13	(20%)
Too early for assessment	39	
Operative deaths	4	(2·7% of whole group)
Later deaths	4	
	150	

operated on within the past three months. All have made satisfactory progress to date, but it is too early to assess the results.

In each case the result was assessed in relation to the pre-operative disability. A good result indicates relief from symptoms such as paroxysmal dyspnoea, orthopnoea, and haemoptysis, and a considerably increased capacity for effort. For example, a more or less bedridden patient is able to sleep flat and to get about in comfort; an ambulant patient whose activities had been much restricted is able to lead a reasonably normal life or to return to work. A fair result implies an obvious and worth-while relief of disability, but short of the optimum improvement. A poor result means slight, doubtful, or no benefit.

Results in Relation to Classification of Cases.—The number of patients in each class is too small to allow of any far-reaching conclusions, but the results indicate a trend. Provided that clinical signs of a pliant diaphragmatic valve are present, the outlook after operation differs little in classes I and II, though in class II the right ventricle is larger and the pulmonary arterial pressure is correspondingly higher. Those in class III have the largest hearts and there is usually a history of recurrent congestive failure; they fare less well and carry a higher operative risk than cases in classes I and II.

SPECIAL FEATURES

Pulmonary Hypertension

The pulmonary arterial pressure by itself does not provide an indication of the degree of mitral stenosis. In cases with paroxysmal pulmonary oedema the mean pulmonary arterial pressure at rest may be little raised, and again in the later stages of mitral disease, when auricular fibrillation and failure have supervened, it need not be greatly elevated. On the other hand, the size of the right ventricle reflects the cumulative effect of pulmonary hypertension on the heart, and is more informative than the level of the pulmonary arterial pressure at a given moment.

The factors responsible for pulmonary hypertension complicating mitral stenosis are beyond the scope of this paper. We were concerned, however, in observing whether pulmonary hypertension influenced the result of mitral valvotomy. The good and poor results in classes I and II were of much the same order, though the degree of pulmonary hypertension was far higher in class II. The outcome of operation was equally favourable in the six patients with the highest pulmonary arterial pressures and greatly increased pulmonary vascular resistance, and in the six with the lowest pressures recorded in this series who had only slightly raised pulmonary resistance (Table III).

TABLE III.—*Mitral Valvotomy: Results in Patients with Highest and Lowest Pulmonary Arterial Pressures*

Series No. of Patient	Mean Pressure (mm. Hg)		Resistance (Dynes/sec./cm.$^{-5}$)		Result
	Pul. Art.	Pul. Capill.	Total Pul.	Pul. Arteriolar	
9	80	—	2,000	—	Good
1	73	—	2,336	—	,,
34	65	30	1,304	704	,,
5	64	25	—	—	,,
53	60	32	—	—	,,
18	59	—	2,048	—	,,
21	32	21	640	216	,,
19	29	—	208	—	,,
44	23	19	376	656	,,
32	22	18	336	92	,,
51	20	12	664	264	,,
26	17	8	416	216	,,

Pulmonary arterial pressure has been measured approximately one year after operation in two patients (Nos. 9 and 1) included in Table III. In both, the mean pressure had fallen, the cardiac output increased, and the total pulmonary vascular resistance lowered by 50% and 60% respectively of their original values. The final figures were still well above normal, yet symptomatic improvement was satisfactory. Similar findings have been reported by other authors (Holling, 1952; Baker, Brock, Campbell, and Wood, 1952).

In mitral stenosis with gross right ventricular enlargement other factors than pulmonary hypertension have to be considered—namely, rheumatic myocardial damage, the effects of auricular fibrillation, and the possibility of associated tricuspid valvular disease.

Rheumatic Myocardial Damage

The relative importance of a defective valve and of rheumatic myocardial damage in the causation of cardiac enlargement and failure is an old-standing problem. Experience of the results of valvotomy has proved that the valvular factor is often far more important than Mackenzie and others believed and taught.

Nevertheless, a grossly enlarged right ventricle implies a damaged myocardium, and whether the damage is rheumatic or whether it is due purely to mechanical stress, it is unlikely to be reversible. The degree of benefit to be expected from valvotomy when the myocardium is permanently damaged is always problematical and the operative risks must be increased. Provided that tricuspid disease is excluded and there are signs of severe mitral stenosis with an operable valve, surgery need not be contraindicated if the age and other circumstances are favourable.

Auricular Fibrillation

So long as the operation was indicated on other grounds, we have disregarded auricular fibrillation entirely in selecting our cases. Indeed, fibrillation offers the advantage of a heart rate controlled by digitalis, whereas in normal rhythm tachycardia may be uncontrollable. In so far as fibrillation is commoner in the advanced than in the early stages of the disease, so those with fibrillation are more often unsuitable for valvotomy than those with regular rhythm. For the same reason the operative mortality would be expected to be higher amongst the fibrillators. Of the entire series of 150 patients, 41% had auricular fibrillation, including three of the four patients who died at operation or within four days of it. Four fatalities occurred later; one of these was fibrillating at the time of operation and three were in sinus rhythm. Otherwise the functional results were as good in those with fibrillation as in those with sinus rhythm.

During the actual valvotomy, bizarre auricular and ventricular arrhythmias were recorded as often in sinus rhythm as in auricular fibrillation.

Auricular fibrillation developed within one to three days of operation in 13 out of 48 patients in sinus rhythm who were operated on at the Middlesex Hospital. In anticipation of this, pre-operative digitalization was carried out as a routine in all cases irrespective of rhythm. In three instances the arrhythmia was related to a small area of pulmonary atelectasis, and sinus rhythm returned promptly when the lung re-expanded. A fourth patient reverted spontaneously before quinidine was given. In seven of the remaining nine cases quinidine restored sinus rhythm, usually after 10 to 15 gr. (0.65 to 1 g.) by mouth; the largest daily dose needed was 30 gr. (2 g.). Post-operative auricular fibrillation was irreversible in two patients. In addition, we have encountered one instance of established auricular fibrillation initiated by cardiac catheterization. Heparin

was given before and during quinidine therapy in two cases, but it is not used as a routine. There has been no instance of embolism related to quinidine therapy. Attempts to abolish post-operative fibrillation with quinidine during the first 10 days after operation were unsatisfactory and resulted in sinus rhythm vacillating with fibrillation. Quinidine is more likely to restore permanent sinus rhythm after the fourteenth day. When auricular fibrillation was established before operation we did not attempt to abolish it, and we have not encountered spontaneous reversion to normal rhythm in such cases.

Embolism

There was a history of embolism in 14 (9%) of the entire series of 150 cases. At operation a thrombus in the left auricle was encountered in only one of these cases (No. 22 —auricular fibrillation); an old adherent clot was dissected away from the appendix with some difficulty. The patient died 12 hours after operation from cerebral embolism. In another case a fatal pulmonary embolism occurred one month after operation.

Post-operative embolism occurred altogether in nine patients; the details are set down in Table IV. Left auricular thrombi were noted at operation in 14 cases; in 11 of these the thrombus was in the appendix and in three in the body of the auricle.

TABLE IV.—*Mitral Valvotomy: Details of Post-operative Emboli in Nine Patients*

Case No.	History of Previous Embolus	Clot in Left Auricle	Site of Post-op. Embolus	Rhythm	Interval after Op.	Clinical Course
17	Yes	No	Pulmonary (multiple)	Recent auric fib.	1 month	Died
22	,,	Yes—in appendix	Cerebral	Auric. fib.	During operation	Died 12 hours later
42	No	No	Pulmonary (multiple)	,, ,,	2 months	Died 5 months after op.
J.O.	,,	?	,,	,, ,,	1 month	Died
46	,,	No	Cerebral	Sinus	During operation	,,
60	,,	,,	Cerebral popliteal	Auric. fib.	,,	Permanent hemiplegia
58	,,	,,	Cerebral	Sinus	,,	Recovery
62	,,	,,	Renal	,,	3 days	,,
87	,,	,,	Cerebral	Auric. fib.	During operation	Permanent hemiplegia

Two patients (Cases 17 and 42) died some months after operation from multiple pulmonary emboli under circumstances which deserve comment. In both patients the operation was technically satisfactory and a good result was anticipated on discharge from hospital. One and three months respectively after operation, during unusually severe foggy weather, they developed bronchitis and rapid auricular fibrillation, complicated by phlebothrombosis of the legs and repeated pulmonary emboli; both developed intractable cardiac failure. The third patient encountered a similar train of misfortunes one month after operation. Death in these three cases followed massive pulmonary embolism. Since this experience we have taken special care to warn the practitioner of the dangers of bronchitis complicating the early post-operative period and of the importance of detecting and treating phlebothrombosis in such patients.

Congestive Cardiac Failure

Congestive (right ventricular) failure had been present at one time or another in 29 of the complete series of 150 patients. Operation was undertaken in these cases only after long deliberation, since factors other than mitral stenosis, such as myocardial damage, might have contributed to the failure to a predominant degree. The majority of them responded favourably to medical treatment, but in a minority (class III) failure was recurrent or a state of borderline failure persisted. The deciding factors in favour of valvotomy were unquestionable signs of a diaphragmatic valve.

The Middlesex Hospital series of 87 cases included 19 with a history of right ventricular failure in whom valvotomy was deemed worth while. In eight of them failure had been related to the onset of auricular fibrillation or an intercurrent lung infection. When the exciting cause was treated the signs of failure disappeared and the heart became smaller, so that these patients were then included in classes I or II. The remaining 11 belonged to class III.

Three of the 19 patients died, one at operation from a tear of the auricular wall and two within a few days of operation. The result of valvotomy was good in four patients and poor in three. The remaining nine have been operated on within the past few months; all have survived, but the interval is too short to allow evaluation of the results. In a few cases the venous pressure increased and oedema developed within 10 days of operation. No cause was discovered, and the signs of failure disappeared spontaneously.

Calcification of the Mitral Valve

A grossly calcified mitral valve is likely to be rigid and is often incompetent. Yet the signs of a pliant diaphragmatic valve may exist with calcification which stands out conspicuously on radioscopy. Calcification was obvious in 9 of the 87 patients treated at the Middlesex Hospital. Small flecks of calcium perceived only after long scrutiny were disregarded. In one instance of gross calcification it appeared that valvotomy would be impossible; yet, because the signs of an operable valve were present, operation was proceeded with. Massive calcification involved the valve ring and invaded the cusps, which, however, were mobile. The commissures were split with ease and the functional result has been gratifying.

In addition to the nine instances of calcification discovered by radioscopy, a further 18 of varying degree were noted at operation, making a total of 27, or 31% of the Middlesex Hospital series. So far calcification by itself has not prevented operation, although often a knife had to be used to split the commissures. Emboli occurred in two of these cases; in one, transient hemiplegia developed after successful splitting of a slightly calcified valve; in the other it followed unsatisfactory widening of a heavily calcified valve.

Associated Valvular Disease

Mitral Incompetence.—Free mitral regurgitation is almost always a contraindication to valvotomy, but we believe that serious incompetence is incompatible with severe stenosis presenting signs of a pliant diaphragmatic valve. In such cases a systolic murmur may be ignored unless there is left ventricular enlargement. Expansile pulsation of the left auricle visible in the anterior view on radioscopy, and evident on both right and left heart borders, should be taken as evidence of significant mitral incompetence. We have seldom found the diagnosis of mitral incompetence a difficult problem except in cases with gross right ventricular enlargement as already discussed.

Aortic Valve Disease.—In the presence of signs of tight mitral stenosis, we have ignored slight and occasionally moderate aortic valve disease. One-third of the Middlesex Hospital cases had aortic incompetence and three of them also had aortic stenosis. However, mitral stenosis was always the dominant lesion. Free aortic incompetence with a thrusting apex beat, a jerky pulse, and left ventricular enlargement contraindicates mitral valvotomy. The result has been good in 15 of the 24 patients with slight aortic incompetence and fair in seven; two have died.

Tricuspid Valve Disease.—The possibility of organic tricuspid disease must always be considered when the right ventricle is greatly enlarged. It should be suspected when the signs of tricuspid regurgitation occur in the absence of congestive failure, when there is a noticeable tricuspid systolic murmur or thrill, and when the right auricle is unduly large. Tricuspid stenosis may sometimes be demonstrated by cardiac catheterization. The absence of pulmon-

ary congestion and relative freedom from dyspnoea and orthopnoea, in the presence of gross right-sided cardiac enlargement, especially if associated with liver swelling and ascites, is characteristic of tricuspid disease. We have regarded this condition as a contraindication to valvotomy. One patient with proved tricuspid stenosis and incompetence was submitted to mitral valvotomy on grounds of her hopeless disability and at her express wish, but unfortunately she died from post-operative embolism, so that the experiment was inconclusive. Functional tricuspid incompetence which disappears when failure responds to treatment is no bar to operation.

Pulmonary Complications

When mitral stenosis is complicated by chronic bronchitis and emphysema it is difficult to decide whether the symptoms are mainly cardiac or pulmonary, and long and careful observation may be necessary. We have performed mitral valvotomy on nine patients with well-marked chronic bronchitis and emphysema; the result was good in two and fair or poor in four. Two died and one case has not been followed up. Two out of three patients with extensive pulmonary haemosiderosis have done well after operation, and the radiological appearance of the lungs has shown a tendency to improve.

Pregnancy

Valvotomy was successfully performed during pregnancy in two patients who developed repetitive paroxysms of pulmonary oedema starting at the third and fourth months. The operation was done in one case at the fourth month, and in the other at the 32nd week, shortly after the patient first came under our care. Great improvement resulted and pregnancy continued normally to term.

Acute pulmonary oedema complicating mitral stenosis is the most important cardiac cause of death actually during pregnancy, and when it occurs after the third month a situation of the utmost gravity arises. Digitalis and other medical measures are unlikely to prevent a recurrence of the attacks if pregnancy continues, so that the choice lies between mitral valvotomy and termination of pregnancy by abdominal hysterotomy. Valvotomy has the double advantage of affording immediate relief to the underlying cause of the pulmonary oedema and of a good chance of preserving the life of the child. Late in pregnancy, however, it must carry a risk of precipitating premature labour in the post-operative period.

We have little doubt that immediate valvotomy is the method of choice in dealing with the emergency which arises when a patient with mitral stenosis develops pulmonary oedema after the third month of pregnancy. This does not imply that, in general, valvotomy renders those with severe mitral stenosis capable of undergoing pregnancy with safety, or that we should encourage such a belief in these patients.

Contraindications to Mitral Valvotomy

The current contraindications, in summary, are as follows:

Age.—Few patients under the age of 20 present with the indications for valvotomy. Because of the danger of activating the rheumatic state, operation should be postponed in these cases unless the symptoms compel immediate surgical relief. We have generally regarded 50 as the upper limit, although six of our patients had passed this age.

Acute Rheumatism.—We have never attempted valvotomy if clinical evidence of acute carditis was present.

Associated Valve Disease.—Predominant aortic valve disease, free mitral incompetence with left ventricular enlargement, and organic tricuspid disease are contraindications to valvotomy.

Myocardial Damage.—This is assessed from the size of the heart and the presence or absence of congestive failure. Gross right ventricular enlargement is a relative contraindication and gross left ventricular enlargement an absolute contraindication to valvotomy. One of our patients who had a coronary occlusion and left bundle-branch block in the electrocardiogram was nevertheless operated on successfully and with benefit.

Pulmonary Disease.—Severe emphysema, chronic bronchitis, and bronchiectasis have proved to be unfavourable.

Congestive Cardiac Failure.—If right ventricular failure cannot be relieved by treatment, mitral valvotomy is unlikely to be successful.

Giant Left Auricle.—Aneurysmal dilatation of the left auricle is often associated with mitral incompetence and with pericardial adhesions. In spite of the huge size of the heart, these patients may remain free from congestive failure for years on digitalis, and their disability is often far less than in cases of severe mitral stenosis with smaller hearts. Valvotomy is contraindicated in such cases.

Anaesthesia for Mitral Valvotomy

Non-explosive agents have been used throughout. Induction and intubation are performed with minimal doses of thiopentone and curare, after which narcosis is maintained by endotracheal gas–oxygen. Approximately 1 g. of procaine hydrochloride in saline is given over the period of an hour by intravenous drip. Topical local analgesic agents are not used. Further small doses of barbiturate and curare are added as required.

Cardiac irregularities of serious import were uncommon and demanded urgent attention on only two occasions. Continuous electrocardiograms, which were taken in the first 30 cases, are now recorded only for special reasons.

Technique of Mitral Valvotomy

The postero-lateral fifth-rib incision is preferred to the antero-lateral, the patient being tilted somewhat towards the supine position. The pericardium is freely opened parallel to the phrenic nerve to expose the lateral aspect of the heart.

Direct auscultation of the heart is carried out with a sterile stethoscope. The auricle and its appendix are gently palpated for thrombi, and if these are absent a light clamp is placed across the base of the appendix. Then, without using any sutures, the tip of the appendix is cut off and the incision enlarged to leave an opening one and a half times the diameter of the surgeon's index finger.

As the clamp is removed the finger is inserted gently. Sometimes the isthmus between the appendix and body of the auricle is unduly narrow and has to be stretched gradually. With the finger now well in the auricle, the tip can be swept over the aortic cusp and carried laterally until the roughened edges of the stenosis are felt. More posteriorly and laterally the wide mouth of the pulmonary vein can be identified. Attention is paid to the following points: ballooning of the antero-medial mitral cusp in ventricular systole, the size of the stenotic opening, the presence of calcification, and the existence of a regurgitant jet.

The actual valvotomy has often been described; it consists in engaging the side of the finger-tip in the opening and trying to fracture the commissures antero-laterally and postero-medially as far as the valve ring, a structure whose presence is inferred rather than felt (Fig. 5).

With the diaphragmatic type of valve, the posterior commissure, which is usually shorter, should be ruptured first; if the anterior commissure is split first, the resulting loss of tension makes the posterior commissure more difficult to deal with. When both commissures have been split (and considerable force may have to be used) the valve cusps are palpated for mobility, the finger is passed down the fan of the chordae tendineae on to the papillary muscles to exclude any cross-fusion, and, finally, a regurgitant jet is again sought for.

The finger is then withdrawn as the auricular clamp is reapplied, and the incision sutured with fine thread. The heart is auscultated again. The pericardium is loosely closed after flushing out with saline, and the chest closed. Temporary water-seal drainage of the chest is maintained for 24 to 48 hours to avoid the effects of a sudden accumulation of pleural fluid.

Matters are not always so straightforward, and the following complications may be encountered:

Auricular Thrombosis.—The incidence of thrombosis in the left auricle or its appendix in this series was 9%. Great caution should be exercised if the auricle does not pulsate and clot is felt within it. The tip of the appendix can be incised and the resultant gush of blood may sweep out a recent clot. Organized clot may be dissected out of the appendix if a light clamp is applied to the base. The danger lies in separating a piece of organized clot as the clamp is applied. If the thrombus is firmly attached, the operating finger may be worked carefully around without disturbing it. A small or thrombosed appendix or a thrombosed auricle may preclude the normal entry, and, if so, access may be gained through the pulmonary vein. The distal branches are held in check ligatures while a clamp is placed at the base of the vein. An oblique incision over the main trunk allows the finger to be introduced, and at the completion of the operation simple suture is used to close the incised vein. In one case the auricular thrombosis was so extensive that it was impossible to introduce a finger or instrument into the heart. The pulmonary vein was too small, and direct incision through the auricular wall showed a thick layer of clot which could not be penetrated.

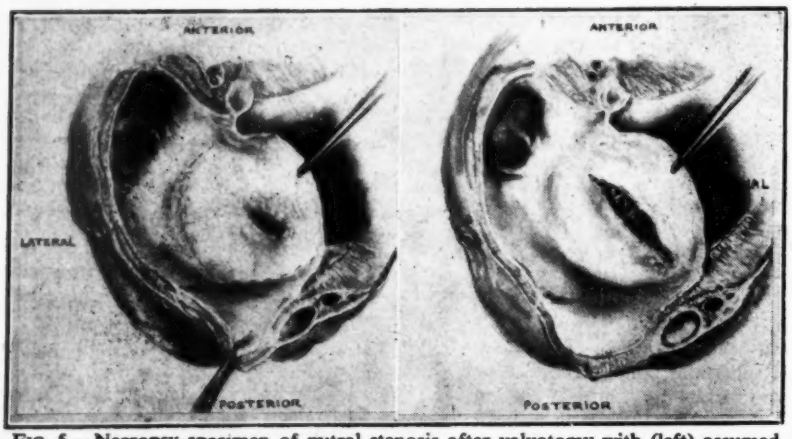

FIG. 5.—Necropsy specimen of mitral stenosis after valvotomy with (left) assumed appearance before operation. The patient (J. O.) died one month after operation from multiple pulmonary emboli.

Embolism.—The separation of clot or calcified fragments may produce embolism in the cerebral vessels, but this is seldom recognized until the patient recovers consciousness. Where a thrombus is palpable in the auricle, the anaesthetist compresses the carotid arteries in the neck during the actual valvotomy. This temporarily arrests the flow into these vessels, and any emboli may be swept along with the active blood flow and avoid the brain. This method is more simple than temporary occlusion of the innominate and left carotid arteries within the thorax.

Tearing of the Auricle.—The incision in the appendix sometimes splits, particularly if the auricular wall is thin. This should be recognized before the finger is withdrawn, as it permits insertion of control sutures before the clamp is applied. The loss of blood from an unsuspected tear can be catastrophic.

Rigidity of the Stenosis.—The finger may fail to rupture the commissure despite the application of considerable force; if so, the greatest care must be exercised to avoid tearing into the aortic cusp or pulling off a papillary muscle. Either of these events may produce a severe regurgitation. If the finger fails, a knife-like instrument attached to the finger can be used, care being taken to avoid injury to surrounding structures.

Haemorrhage.—In a straightforward operation the loss of blood does not exceed 1–2 oz. (28–57 ml.). If much manipulation is required or if the auricular wall is torn, urgent measures are necessary to replace the blood loss. A routine intravenous drip may be adequate for a moderate haemorrhage, but transfusion direct into the left ventricle or aorta is needed if a pint (570 ml.) or more is suddenly lost. This had to be undertaken on one occasion in our series.

Influence of Technical Result of Operation on Functional Result

An assessment has been made of the technical result of each valvotomy performed. When free splitting of the commissures was achieved without producing incompetence, 84% of the patients obtained a good functional result, compared with only 46% when the valvotomy was less complete. If the tiny slit of the stenosis is enlarged even by a few square millimetres, the volume of blood passing through the valve may be considerably increased. This may account for the early benefit experienced by certain patients in whom the technical result of the operation was poor in so far as the commissures were split to only a limited degree or a funnel-shaped valve could be merely dilated by the finger.

Summary and Conclusions

The basic indication for mitral valvotomy is disability from mitral stenosis of an anatomical form which is amenable to surgical correction. This type of stenosis, in which there is a *pliant diaphragmatic valve*, gives rise to characteristic clinical signs by which it may be recognized and which are described.

The most important consequence of pulmonary hypertension is right ventricular enlargement, and the size of the right ventricle, as determined by clinical, radiological, and electrocardiographic findings, provides a more valuable index to the degree of pathological change due to mitral stenosis than does the level of the pulmonary arterial pressure at a given moment. Cardiac catheterization is no longer required as a routine measure in the selection of cases suitable for mitral valvotomy. Selection may now be made on a basis of the symptoms and of the data provided by routine cardiological examination.

Mitral valvotomy has been performed on 150 patients, of whom 31 were men and 119 women. Their ages ranged from 19 to 57 years. Four patients died as a direct result of the operation, an immediate mortality of 2.7%. Four died from various causes some time after the operation.

The results in 111 patients followed up for five months to two and a half years have been good in 74% and only fair or poor in 20%. Patients with auricular fibrillation (41% of the series) did as well as those in sinus rhythm, but three of the four operative fatalities were in fibrillation.

Cases selected for operation on grounds of an operable valve were classified according to the size of the right ventricle and the presence of congestive failure. Patients with large hearts, and congestive failure which failed to respond to treatment, benefited least from valvotomy. When free splitting of the commissures was achieved, 84% of the patients obtained good symptomatic relief, whereas when valvotomy was judged at operation to be less satisfactory only 46% of good results were obtained. Nevertheless, partial splitting of the valve does not preclude satisfactory clinical improvement.

Good results were obtained alike in those with greatly elevated pulmonary arterial pressures and in those with a slight or moderate elevation.

The following are regarded as contraindications to operation : active rheumatic carditis, severe myocardial damage as revealed by gross right ventricular enlargement and intractable congestive failure, predominant aortic valve disease, organic tricuspid valve disease, mitral incompetence associated with left ventricular enlargement, and a giant left auricle. Chronic bronchitis, emphysema, and other pulmonary complications prejudice the success of the operation.

The technical details of mitral valvotomy and the operative complications are briefly described.

We wish to thank many colleagues in hospital and in practice, particularly Dr. K. Shirley Smith and others at the London Chest Hospital, who have kindly referred patients needing valvotomy. We are especially indebted to Mr. J. R. Belcher, who has taken an active part in the surgical management of the Middlesex Hospital patients.

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CHLORAMPHENICOL TREATMENT OF BRONCHIECTASIS IN CHILDREN

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Although most acute bacterial infections are now readily amenable to chemotherapy the problem of chronic infection based on structural changes remains unsolved. Whatever the prime cause or causes of bronchiectasis, the main symptoms in childhood result from chronic or recurrent infection of damaged lung. The damage is almost certainly permanent, yet follow-up studies suggest that the infection, as evidenced by clinical signs and symptoms, may die out towards adolescence. Cultures of sputum show the frequency of infection with *H. influenzae*, and, as this is an organism highly susceptible to chloramphenicol, a study has been made of the effect of this drug on the course of bronchiectasis. The study has been brought to an end by the recognition of the possible dangerous action of chloramphenicol on bone marrow. Sufficient knowledge had already been gathered to shed light on two problems—the nature of the infection, and the response, bacteriological and clinical, to chemotherapy ; and these observations are reported here.

Clinical Material

Thirty-six cases of bronchiectasis in all, aged 3 to 15 years, have been treated with chloramphenicol. Judged by the quantity of sputum obtained while the patients were being treated by physiotherapy, 22 were severe and 14 were mild cases. Fifteen cases were able to produce an indefinite amount of sputum, 10 with involvement of at least four lobes. Among eight unilobar cases, only two are included in the severe group.

The first observations concern 15 cases, aged 5 to 10 years, in the Meath School of Recovery at Ottershaw (Invalid Children's Aid Association). In 11 the sputum grew *H. influenzae* alone, and in four *H. influenzae* with pneumococci. All had first been treated by a physiotherapist for many weeks, and eight of the cases could cough up a limitless quantity of purulent sputum at any time during the day. The dose of chloramphenicol was 500 mg. eight-hourly in capsules by mouth, equivalent to between 20 and 30 mg. per lb. (44 and 66 mg. per kg.) body weight daily. The quantity of sputum lessened dramatically, and by the third or fourth day of treatment it became difficult to obtain a specimen ; cultures were sterile.* After seven days the drug was stopped in 10 and continued in five of the cases. The mildest case had no more sputum after this week of treatment and remained well and symptom-free for a whole year following discharge home. In the other nine cases sputum cultivated on the sixth day after the end of treatment showed a return of the original organism, while sputum from the five cases still under treatment remained sterile in four and grew pneumococci in one. Two cases continued treatment at half the original dose for two further weeks, the sputum remaining sterile, while two very severe cases, treated on half the original dose for five and six months, later increased the quantity of sputum to ½ to 1 oz. (14 to 28 ml.) daily (compared with 6 to 8 oz. (170 to 230 ml.) collected easily before treatment) and the sputa grew bacteria from time to time, but never *H. influenzae*. In all the severe cases *H. influenzae* regained its ascendancy in the sputum within 10 days of the end of treatment, though cough and the quantity of sputum were less than before treatment began.

Three cases had 250 mg. of chloramphenicol twice a day for one, two, and five months (approximately 10 mg. per lb. (22 mg. per kg.) daily), and pneumococci, streptococci, and staphylococci appeared from time to time without *H. influenzae*. In seven cases three doses of 250 mg. eight-hourly for one day of each week were given for one month in one case, for three months in five cases, and for five months in one case (12 to 24 mg. per lb.: 26 to 53 mg. per kg.). Cultures of sputum were sterile on the day after treatment, but grew various bacteria, including *H. influenzae*, by the sixth day, so that weekly treatment failed to produce constant sterility of the sputum. Assessment of the 15 cases one year after starting treatment showed a maintained improvement in seven ; two are somewhat better, and in the six clinically most severe cases lessening of the sputum occurred only while chloramphenicol was actually being given.

A second observation at the Meath Home concerned eight patients from 3 to 8 years old. Six sputa grew *H. influenzae* and one sputum grew *H. influenzae* with *N. catarrhalis*. In one case there was a pure growth of pneumococci, and this is the only case in the study from whose sputum *H. influenzae* was not grown. Six cases were given 250 mg. eight-hourly for 18 days (13 to 21 mg. per lb. (29 to 46 mg. per kg.) daily). On this dose, two-thirds of that given in the previous test, there was the same dramatic change in the quantity and character of the sputum from the third or fourth day, with the same return of organisms within a few days of the end of treatment. Sputum from

*This term is used for the sake of brevity to describe cultures containing no colonies of any pathogen and very few colonies of commensals.

four of the cases given the same daily dose twice a week was not kept sterile.

Only two children, both with extremely severe symptoms, aged 3½ and 4 years, were given chloramphenicol palmitate, at first in doses of 12 and later of 24 mg. per lb. (26 and 53 mg. per kg.) daily, but the sputum failed to lessen in quantity or to become sterile in either. The death of one of these patients is referred to later.

Thirteen other cases of bronchiectasis have been treated with chloramphenicol capsules by mouth in the wards of St. Bartholomew's Hospital and Osterhills Hospital, St. Albans. Ages ranged from 4 to 15 years, eight cases being severe and five mild. Again *H. influenzae* was the predominant and usually the only organism cultivated from the sputum, and again daily doses of 12 to 15 mg. per lb. (26 to 33 mg. per kg.) sterilized the sputum in three or four days, with the same recurrence after treatment, the more rapidly the severer the case. The five mild cases have been treated periodically with one or two weeks of chloramphenicol—20 mg. per lb. (44 mg. per kg.) daily divided into three doses—particularly at the time of any acute respiratory symptoms; and under this regime school life and health have been little upset.

The following laboratory data are based on findings in 27 of the cases here described, examination in the remainder not having been performed by one of us (L. P. G.).

Sputum Findings

The characters of the sputum in these patients were strikingly uniform. It consisted of thick yellow odourless mucopus. Except in the one case, already noted, which had a pure pneumococcus infection, a stained film invariably showed large numbers of minute Gram-negative rods, and culture gave a growth consisting almost entirely of *H. influenzae*. The only other identifiable pathogen in the sputum of untreated cases was *Str. pneumoniae*: this was found in 10 cases, but in relatively very small numbers.

Sensitivity to Antibiotics of Strains of H. influenzae from Cases of Bronchiectasis

Antibiotic	Total No. of Strains	Minimum Inhibitory Concentrations (μg./ml.)					
		0·25	0·5	1	2	4	8
Chloramphenicol ..	37*	2	16	19			
Penicillin	22		2	15	3	1	1
Streptomycin ..	22			3	2	16	1
Aureomycin ..	22	2	3	17			
Terramycin ..	22	1	8	13			

Figures are numbers of strains inhibited by each concentration.
* Includes 10 strains from similar but untreated cases.

The sensitivity of the strains of *H. influenzae* to chloramphenicol and other antibiotics is stated in the Table. These determinations were made by incorporating the antibiotic in falling dilutions (two-fold differences) in plates of heated blood agar, the surface of which was inoculated with a small loopful of heated blood-broth culture, diluted approximately 1:500, in each of eight areas—that is, eight strains per plate were tested. The concentrations stated are those completely inhibiting growth after 24 hours: the next lower always showed diminished growth and the next full growth. All the strains tested were inhibited by 1 μg./ml., 16 by 0.5 μg./ml., and 2 by 0.25 μg./ml. of chloramphenicol.

The further tests with other antibiotics were done later with 22 strains which had been preserved in the dried state, the same method being used.

The sputum of patients under adequate treatment with chloramphenicol was distinguishable at a glance from a pre-treatment specimen. It was white in colour and less cellular, contained no *H. influenzae*, and at first yielded no significant growth. Two other species tended to appear during treatment: *Str. pneumoniae* (in 11 patients), which was shown in three patients whose sputum had originally contained it in small numbers to have diminished in its sensitivity to chloramphenicol; and a chloramphenicol-resistant *Staph. pyogenes*. Sputum containing these organisms became more cellular, but in neither purulence nor quantity did it attain the characters of pre-treatment sputum.

Estimations of Drug in Sputum.—A method for this was devised, depending on two convenient facts: that chloramphenicol is heat-stable, and that the air passages and mouth usually contain no sporogenous or other heat-resistant bacteria. Specimens were accordingly placed in a water-bath at 60° C. for one and a half hours, then diluted 2-, 4-, 8-, and 16-fold in heated blood broth, and inoculated with *H. influenzae* itself. The organism grew well in all dilutions of control tests with non-drug-containing sputum, and was inhibited to the expected dilution in control tests in which chloramphenicol had been added. Whether the inoculum had multiplied was determined by plating after one day's incubation.

The results of such tests in 15 specimens showed the presence of 8 μg./ml. chloramphenicol in five and 4 μg./ml. in six who were receiving chloramphenicol, and less than 2 μg./ml. in four specimens from two patients receiving chloramphenicol palmitate, in whom this compound had failed to eliminate *H. influenzae* from the sputum.

Acquired Bacterial Resistance

Habituation to chloramphenicol was attempted *in vitro* by repeated transfers in heated blood broth containing increasing concentrations. Of three strains of *H. influenzae*, two showed a fourfold and one a twofold increase after five transfers. Of three strains of *Str. pneumoniae* two showed a fourfold increase and one no change after 10 transfers. Each of three strains of *Staph. pyogenes* underwent a fourfold increase in resistance in 10 transfers.

Acquired resistance *in vivo* was observed with three strains of *Str. pneumoniae*, the difference being fourfold in each case (inhibitory concentration increasing from 2.5 to 10 μg./ml.), and in three strains of *H. influenzae*, originally inhibited by 0.25, 0.5, and 0.5 μg./ml., and found after treatment in each case to require 2.0 μg./ml. One of these patients was given diminishing doses, which eventually failed to suppress the infection, and two were treated with chloramphenicol palmitate, which also failed to eliminate the organism. There is thus some suggestion that inadequate treatment tends to encourage the acquisition of bacterial resistance.

Toxic Effects

One patient, a female aged 4 years, was given 125 mg. of chloramphenicol palmitate three times a day for 20 days, followed by 250 mg. thrice daily for 29 days (total, 29.25 g.). Pallor was noted at the end of this course: eight days later there was generalized purpura. Despite vigorous treatment she died with multiple haemorrhages and an aplastic marrow 26 days after the appearance of purpura. (We are permitted by our colleague, Professor R. V. Christie, to mention that an aplastic anaemia also developed in a man under his care who had had prolonged chloramphenicol treatment for *H. influenzae* bronchitis: this patient, after many transfusions, is apparently recovering.)

Discussion

The effects of chloramphenicol when 20 mg. per lb. (44 mg. per kg.) is given by mouth daily, divided into three doses, is consistently to diminish the quantity of sputum and to sterilize it in three or four days. Continued treatment may be accompanied by a later increase in the quantity of mucoid sputum up to 2–3 oz. (57–85 ml.) daily despite the absence of pus and bacteria. The abnormal physical signs characteristic of active infection persist even when sputum disappears altogether. Bacteria reappear when the dose drops below 20 mg. per lb. per day or is

given less often than eight-hourly. Pneumococci and staphylococci seem to reappear during long courses of treatment, but not to persist. In most cases, once the *H. influenzae* returns the other invading bacteria quickly die out. Mild and unilobar cases may remain symptom-free for many months after a course of two weeks' treatment (eight cases). Severe cases have always relapsed within 10 days of ceasing treatment, and sometimes the relapse is heralded by an acute febrile illness lasting one or two days. In every case another course of treatment has produced another remission. The question arises whether in severe cases the *H. influenzae* remains deep in the tissues of the bronchiectatic lung, ready to reappear in the sputum when the drug is stopped, or whether reinfection occurs. The larger doses that might reduce the risk of relapse on the first hypothesis have not been regarded as safe in these observations.

Unfortunately the possibly toxic effect of chloramphenicol on bone marrow, responsible for one death in the cases treated in this series, makes the prolonged use of the drug unwise. Some of the cases reported here have taken as much as 100 g. in six months without apparent ill effect, and repeated blood examinations might give warning of trouble in time for the drug to be stopped, before changes in the marrow become irreversible. *We do not, however, intend to persist with this treatment.* We feel that our results must be recorded to show that there is a place—if now vacant—in the medical treatment of bronchiectasis in children for an antibiotic sharing with chloramphenicol the power of rapidly reaching a high enough concentration in the respiratory tract to destroy *H. influenzae* without inducing resistance, so that recurrent infection may be successfully treated in the same way. Such a drug would combine safety with the power to dry up sputum and to make bacteriologically safe surgical procedures on lower respiratory tract or on upper respiratory tract, so often the site of disease causing persistence of symptoms; secondly, would be suitable for routine preventive treatment in severe bronchopneumonia in infancy, especially in association with pink disease and whooping-cough; thirdly, would keep the mild unilobar case free from recurrences following intercurrent influenza or other acute respiratory infections; and, fourthly, would give periods at least of freedom from endless cough and sputum in the severest cases where five lobes are diseased in early childhood, and where even the boldest thoracic surgeon must refuse surgical help. For those who believe that *H. influenzae* is responsible for the persistence of symptoms in the majority of cases of bronchiectasis, and that bronchiectasis is a disease with a tendency towards improvement and dying out of symptoms in time, the situation urgently demands a safe antibiotic with the remarkable powers of chloramphenicol. Our experience with aureomycin and terramycin, to which *H. influenzae* is also very sensitive, is so far too limited to justify any report.

Summary

Of 36 cases of bronchiectasis in children a pure or almost pure infection by *H. influenzae* was present in 35.

Chloramphenicol, to which this organism is highly sensitive, invariably produced a remission while being given in adequate doses. After cessation of treatment, severe cases reverted to their original condition, but some milder ones appeared to have received more lasting benefit.

One patient died of aplastic anaemia, an occurrence which led to the abandonment of the treatment.

We are indebted to Miss Pamela M. Waterworth for skilled laboratory assistance, and to Miss Gosling and her staff at the Meath School of Recovery for collecting and personally conveying to London many specimens of sputum.

THE IN-VITRO SENSITIVITY OF H. INFLUENZAE TO FIVE DIFFERENT ANTIBIOTICS

BY

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At times clinicians find it difficult to select and bacteriologists to suggest the antibiotic most effective in some of the less common bacterial infections until detailed sensitivity tests have been carried out, with the result that there is a delay of at least 24 hours in administering the one regarded as most suitable.

This situation occurs particularly often in infections due to *Haemophilus influenzae* (Mulder, 1952). This organism causes both acute infections—for example, meningitis, obstructive laryngo-tracheobronchitis, pneumonia, empyema (Rivers, 1922; Alexander, 1943; Zinnemann, 1947), and also chronic infections with acute exacerbations, such as otitis, sinusitis, and bronchiectasis (Hirsch, 1912; Mulder, 1940; Allison, J. Gordon, and Zinnemann, 1943; Bjuggren and Tunevall, 1952; Tunevall, 1952). It is sensitive in some degree to all antibiotics easily available in this country (M. Gordon and Zinnemann, 1945; Hewitt and Pittman, 1946; Alexander, Leidy, and Redman, 1949).

Few comparative assessments of the more recent antibiotic drugs against *H. influenzae* have been made, and these mostly on a small number of strains (Alexander *et al.*, 1949; Long *et al.*, 1950; McCrumb *et al.*, 1951; Schoenbach *et al.*, 1952). Recently two larger series have been published (Mulder *et al.*, 1952; Tunevall, 1951): see Table I. Mulder *et al.* recorded only the upper and lower limits of the minimal *in-vitro* inhibiting doses for *H. influenzae* as did all authors quoted above, with the exception of Tunevall, whose findings will be discussed in detail later. The results obtained have not led any of the authors to make specific recommendations for the choice of an antibiotic drug in *H. influenzae* infections. The figures of Mulder *et al.*, however, are slightly favourable to chloramphenicol, whereas those of Tunevall suggest aureomycin.

TABLE I.—*Minimum Inhibitory Concentrations of Antibiotics for H. influenzae, Expressed in µg. per ml. of Medium in vitro, as Determined by Various Authors*

Authors	Penicillin	Streptomycin	Aureomycin	Chloramphenicol	Terramycin	Total No. of Strains Tested
Alexander *et al.* (1949)	N.T.	1–3	0·5–1	1	N.T.	?
Long *et al.* (1950)	,,	1·25	0·625–2·5	N.T.	2·5	2 (C)
McCrumb *et al.* (1951)	0·8–10	0·8–10	0·4–10	0·4–5	1·7–2·5	16 (C)
Schoenbach *et al.* (1952)	0·156–10	1·56–3·1	0·156–2·5	0·156–5	0·156–5	22 (C)
Mulder *et al.* (1952)	0·35–2·8*	0·5–8	N.T.	0·25–3	5·8	14–187 (N)
Tunevall† (1952)	0·35–2·8*	0·25–4	0·063–0·5	0·063–0·5	0·063–0·5	21 (C) 42 (N)

N.T. = Not tested. (C) = Capsulated strains. (N) = Non-capsulated strains.
* Figure arrived at by conversion of Oxford units to micrograms.
† Author records number of strains and percentages inhibited by serial twofold dilutions within the limits quoted in this table.

During our routine determinations of the sensitivity of *H. influenzae* strains to antibiotics the impression was

obtained that chloramphenicol was more effective than the rest. To confirm this impression capsulated and non-capsulated strains of *H. influenzae* isolated from pathological conditions during the period January 1, 1951, to October 30, 1952, and a number of strains of both varieties from similar routine material kindly forwarded by Dr. K. B. Rogers, of the Children's Hospital, Birmingham, were tested by the standard method described below, and the results analysed. The data were collected as strains became available.

Technique.—As soon as possible after isolation the strains were inoculated into Levinthal broth and incubated overnight. Four drops of a 1 in 1,000 nutrient-broth dilution of this culture were spread uniformly over the whole surface of each of three heated horse-blood (chocolate) agar plates. With a sterile cork-borer a number of holes were punched at regular intervals in the medium around the edge of the plates. The holes were filled to within about 1 mm. of the rim with the dilutions of the antibiotic drugs. Penicillin was tested by itself on the first plate; streptomycin was paired with aureomycin on the second, and chloramphenicol with terramycin on the third plate. The standard dilutions of antibiotics employed were 1 μg., 2 μg., 5 μg., and 10 μg., except for penicillin. Of the last-named drug 1, 2, 5, and 10 Oxford units (corresponding to 0.61, 1.22, 3.05, and 6.1 μg.) were used. After overnight incubation the plates were read and the results recorded.

Definitions.—Some investigators have based their readings on partial, others on complete inhibition (Jackson and Finland, 1951). Results of the two methods arrive at different values. To facilitate comparison with the findings of other workers the results for both methods of reading are given in Tables IV and V. In this investigation the term "partial inhibition" is not based on any measurements of the width of inhibition zones but indicates a marked zone of inhibition of growth around the punch-holes with slight growth still occurring inside the zones and right up to the edge of the punch-holes. The term "complete inhibition" indicates complete absence of growth within the whole or part of the inhibition zone.

Results

A total of 34 capsulated and 50 non-capsulated strains of *H. influenzae* were investigated. All these strains were isolated from cases in which *H. influenzae* was present as the only or predominant bacterium and in which it appeared that the clinical conditions were related to or aggravated by this organism. Tables II and III give details of the sites from which the strains were isolated and the number of strains isolated from these sites. As was to be expected, the majority of capsulated *H. influenzae* strains were obtained from the cerebrospinal fluid of cases of meningitis in children, and all 21 strains from this site were of type b (Pittman). The possible sources of non-capsulated strains are fairly well represented by the 50 strains investigated. All strains may thus be regarded as unselected.

TABLE II.—*Distribution of 34 Capsulated H. influenzae Strains According to Types and to Sites from which Isolated*

Site	No. of Type Strains Isolated					
	a	b	c	d	e	f
Cerebrospinal fluid ..	0	21	0	0	0	0
Blood culture	0	2	0	0	0	0
Bronchial secretion ..	0	2	0	0	0	0
Nasopharynx	0	2	1	0	1	0
Sputum	0	0	0	1	0	0
Trachea at necropsy ..	0	0	0	0	2	0
Ankle-joint	0	1	0	0	0	0
Conjunctival sac ..	0	1	0	0	0	0
Total	0	29	1	1	3	0

TABLE III.—*Distribution of 50 Non-capsulated H. influenzae Strains According to Sites from which Isolated*

Site	No. of Strains Isolated
Blood culture	3
Bronchial secretion ..	9
Sputum	3
Throat	8
Nose	4
Nasopharynx	6
Antrum	6
Ear	3
Conjunctival sac	5
Pleural cavity (empyema) ..	3
Total ..	50

A more exacting test is the *in-vitro* determination of the concentration of any given antibiotic required to inhibit a micro-organism completely. Table IV shows that in such a test 1 unit per ml. of chloramphenicol inhibits completely one-quarter of the capsulated and two-fifths of the non-capsulated *H. influenzae* strains, while all other antibiotics tested inhibit only 6% or less of all the strains. At a concentration of 2 units per ml. chloramphenicol inhibits one-half of the capsulated and over four-fifths of the non-capsulated strains, while none of the other antibiotics inhibits completely more than roughly one-quarter of the capsulated and one-sixth of the non-capsulated strains. All of the capsulated strains, with one exception, and 100% of the non-capsulated strains are completely inhibited by 5 units per ml. of chloramphenicol, while the most effective of the other antibiotics inhibit only three-quarters of the strains at this concentration. The effective concentrations are naturally lower if partial inhibition is used as the basis to assess antibiotic activity (Table V).

Terramycin and penicillin follow chloramphenicol fairly closely in their *in-vitro* performance against *H. influenzae*, and it would be difficult, on the basis of the figures obtained, to decide which of these two drugs is more active. Streptomycin and aureomycin appear to be roughly equal but less inhibitory than terramycin and penicillin, particularly as judged by the partial inhibition test.

Discussion

The superiority of chloramphenicol in inhibiting *H. influenzae in vitro* in these investigations is somewhat surprising in view of the absence of similar statements in the not inconsiderable literature on the drugs tested, although chloramphenicol and aureomycin have now been in use for five and terramycin for three years. Clinically, however, infections due to Gram-negative organisms have been reported to respond better to chloramphenicol (McCrumb *et al.*, 1951). Jackson and Finland (1951) drew attention to the fact that determinations of *in-vitro* sensitivity to antibiotics carried out with diverse methods and in the hands of different investigators cannot easily be compared and that the conclusions reached may differ. Such divergencies in tests on *H. influenzae* are shown in Table I. The argument does not seem entirely valid if used against the results reported in this communication, for the following reasons.

Table I, which summarizes the principal papers on the sensitivity of *H. influenzae* to antibiotics, shows that, with the exception of one (Tunevall), the authors have confined themselves to indicating the upper and lower limits of the minimal inhibiting doses of the antibiotics investigated. In the results here reported the figures have been analysed in such a way as to record the number of strains of *H. influenzae* inhibited at four concentrations of five different antibiotics. This method of tabulating results is better suited to stressing the superiority of one or the other of the drugs investigated. Results similar to the ones reported here have been obtained by an independent observer (W. Goldie, personal communication, 1952). However, Tunevall (1952) recorded his findings in a way closely resembling the one used in this communication. In his Table I there is a suggestion of a slight superiority of aureomycin over chloramphenicol, although in his conclusions the author regards the two drugs as equally effective. The explanation for the divergence between the two sets of experiments may perhaps be found in the different

techniques used, as Jackson and Finland (1951) suggested. Tunevall incorporated the antibiotics in serial twofold dilutions in a solid medium, which was then inoculated with the strains to be tested, while the present findings are based on the punch-plate technique.

As a rule determinations of sensitivity carried out in fluid media or with the antibiotic incorporated in a solid medium tend to give lower values than those obtained with the punch-plate method. It may be inferred from this fact that the actual inhibitory concentrations of all antibiotics tested in the way here described are lower than appears from the findings recorded. However, the order of effectiveness should not be influenced by lower readings.

Ease of administration favours the so-called broad spectrum antibiotics, but side-effects such as gastro-intestinal irritation may sometimes make their administration difficult if not impossible, quite apart from the uncertainty about the doses given if vomiting occurs. In practice, blood concentrations of penicillin high enough to inhibit most or all *H. influenzae* strains are difficult if not impossible to achieve and to maintain, although such concentrations can be obtained easily in the C.S.F. by intrathecal injection. On the other hand, therapeutically effective blood concentrations of the order of 5 to 10 μg. are the rule with usual oral doses of chloramphenicol, aureomycin, and terramycin, or with intramuscular doses of streptomycin (Zintel *et al.*, 1945; Ehrlich, 1947; Dowling *et al.*, 1948; Glazko *et al.*, 1949; Welch, 1950; Eads *et al.*, 1952). It is evident, therefore, that the quite impressive *in-vitro* performance of penicillin is not likely to be equalled by its performance in clinical infections due to *H. influenzae*, except in some conditions, such as meningitis (Zinnemann, 1946) or empyema, where a high concentration of the drug can be applied locally. This circumstance still further emphasizes the value of chloramphenicol in *H. influenzae* infections, with terramycin as a good second best. Aureomycin is a difficult drug to assess in *in-vitro* experiments, as up to 50% of its activity may be lost during incubation at 37° C. (Chandler and Bliss, 1948). It is possible, therefore, that the *in-vivo* activity of aureomycin against *H. influenzae* is greater than is suggested by the *in-vitro* results given in Tables IV and V. However, observations on patients with chronic infections due to *H. influenzae* (Allibone, 1953, personal communication) seem to agree well with the *in-vitro* results reported here, the order of *in-vivo* effectiveness being chloramphenicol, terramycin, and aureomycin. It must be stressed, though, that *in-vitro* sensitivities to antibiotics do not necessarily permit conclusions on the effectiveness of these drugs *in vivo* in spite of good agreement in this series.

In view of the greater inhibitory action of chloramphenicol on *H. influenzae* it is unfortunate that this drug is claimed to cause aplastic anaemia and related blood dyscrasias (Volini, *et al.*, 1950; Gill, 1950; Smiley *et al.*, 1952). Sturgeon, 1952; Rheingold *et al.*, 1952; Hawkins and Lederer, 1952; Wolman, 1952; Hargraves *et al.*, 1952). Probably no great harm will be done if chloramphenicol is used for one short course of a few days' duration. Repeated or prolonged administration seems to be the common feature of most of the cases of blood dyscrasias reported hitherto, though a few cases have been described with granulocytopenia following one short course of the drug (Gill, 1950; Volini *et al.*, 1950). Hargraves *et al.* (1952) attribute the deaths from aplastic anaemia of two of the cases reported by them to comparatively small doses of chloramphenicol, but there is an element of doubt in the history of administration of the drug.

Thus it would appear that the antibiotic having the best *in-vitro* and *in-vivo* inhibitory action against *H. influenzae* may have limitations in practical application. More evidence for or against the prolonged or intermittent administration of chloramphenicol is required to assess its value in the therapy of chronic infections due to *H. influenzae*.

Summary

The *in-vitro* antibiotic action of penicillin, streptomycin, aureomycin, chloramphenicol, and terramycin on 34 capsulated and 50 non-capsulated *H. influenzae* strains has been tested at four concentrations. The punch-plate method was used for these sensitivity tests.

Chloramphenicol is the only one of the antibiotics tested which is capable of inhibiting 100% of the strains investigated at the comparatively low concentrations

TABLE IV: COMPLETE INHIBITION.—*In-vitro Sensitivity of H. influenzae Strains to Antibiotics. Punch-plate Method on Heated Blood (Chocolate) Agar Plates; Units/ml.=Oxford Units in the Case of Penicillin and μg. in the Case of All Other Antibiotics*

Antibiotic Drug	Capsulated Strains: No. and Percentage of Strains Inhibited by Units/ml. 1	2	5	10	Total No. of Strains Tested	Non-capsulated Strains: No. and Percentage of Strains Inhibited by Units/ml. 1	2	5	10	Total No. of Strains Tested
Penicillin ..	0	8 (23·5%)	17 (73·5%)	9 (100%)	34	3 (6%)	3 (12%)	29 (70%)	14 (*1*) (98%)	50
Streptomycin ..	1 (2·9%)	3 (11·8%)	16 (58·8%)	11 (*3*) (91·1%)		1 (2%)	7 (16%)	26 (68%)	10 (*6*) (88%)	
Aureomycin ..	1 (2·9%)	3 (11·8%)	10 (41·2%)	13 (*7*) (79·4%)		2 (4%)	1 (6%)	17 (40%)	24 (*6*) (88%)	
Chloramphenicol	8 (23·5%)	9 (50·0%)	16 (97·0%)	1 (100%)		20 (40%)	22 (84%)	8 (100%)	—	
Terramycin ..	0	1 (3·0%)	23 (72·7%)	7 (*2*) (93·9%)	33	1 (2%)	3 (8%)	33 (74%)	12 (*1*) (98%)	

Figures in parentheses indicate number of strains not inhibited by 10 units/ml.
Plain figures indicate absolute number of strains inhibited by a particular concentration of a particular antibiotic; percentage figures indicate proportion of *all strains* inhibited by a particular concentration of antibiotic drug.

TABLE V: PARTIAL INHIBITION.—*In-vitro Sensitivity of H. influenzae Strains to Antibiotics. Punch-plate Method on Heated Blood (Chocolate) Agar Plates; Units/ml.=Oxford Units in the Case of Penicillin and μg. in the Case of All Other Antibiotics*

Antibiotic Drug	Capsulated Strains: No. and Percentage of Strains Inhibited by Units/ml. 1	2	5	10	Total No. of Strains Tested	Non-capsulated Strains: No. and Percentage of Strains Inhibited by Units/ml. 1	2	5	10	Total No. of Strains Tested
Penicillin ..	8 (*3*) (23·5%)	15 (76·5%)	8 (100%)	—	34	5 (*1*) [3] (10%)	21 (*8*) (54%)	13 (*1*) (96%)	1 (100%)	50
Streptomycin	3 [1] (8·8%)	14 (*3*) (50·0%)	10 (*1*) (79·4%)	2 (97·0%)		5 (*3*) [1] (10%)	21 (*5*) (58%)	9 (*1*) (86%)	3 (94%)	
Aureomycin	4 (*1*) [1] (11·8%)	9 (41·2%)	13 (79·4%)	5 (94·1%)		3 [2] (6%)	17 (40%)	24 (88%)	5 (98%)	
Chloram-phenicol ..	17 [8] (50·0%)	15 (*1*) (94·1%)	1 (100%)	—		41 (*1*) [20] (82%)	8 (100%)	—	—	
Terramycin..	2 [1] (6·1%)	18 (*4*) (60·6%)	7 (93·9%)	2 (100%)	33	4 [1] (8%)	31 (*2*) (70%)	12 (98%)	1 (100%)	

Figures in parentheses = number of strains partially not inhibited at given but completely inhibited at next higher concentration.
Figures in square brackets = number of strains not tested at < 1 unit/ml.
Plain figures indicate absolute number of strains inhibited by a particular concentration of a particular antibiotic; percentage figures indicate proportion of *all strains* inhibited by a particular concentration of antibiotic.

obtained with the usually recommended therapeutic doses. Terramycin comes next in order of effectiveness, followed by streptomycin and aureomycin. Penicillin *in vitro* is as effective as chloramphenicol and terramycin, or even better, on a weight-for-weight basis, but blood concentrations within the effective range are difficult to obtain and maintain.

Deterioration of aureomycin at 37° C. may be responsible for the comparatively low rating of the drug, but clinical impressions in chronic *H. influenzae* infections also suggest the superiority of chloramphenicol.

I am indebted to the Medical Research Council for a grant in aid of expenses.

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The Home Office has recently issued the report of the Commissioners of Prisons for 1952 (Cmd. 8948). It deals with the administration of prisons; statistics of the prison population; the treatment, training, and after-care of prisoners; Borstal training; detention centres; and the health of prisoners. In spite of the serious overcrowding in the prisons, there was no epidemic of infectious disease last year, and even the usual outbreaks of influenza in the early months were conspicuously absent at most establishments. Indeed, the director of medical services notes, as an interesting observation, that during past influenza epidemics, where three men have shared a cell and one has developed the disease, the infection not infrequently has spread to men in neighbouring cells, while others in the original cell may escape it altogether. However, the potential risk to health consequent on overcrowding is constantly in the minds of the prison medical officers. In August, 1952, the first detention centre for boys of 14 to 17 years was opened, and the medical officer reports that the training there has had a beneficial effect on the physique and health of the boys admitted. The idea of the centre is to provide an alternative to prison for young offenders who do not need prolonged Borstal training yet are unlikely to respond to probation.

THE PROGNOSIS AND ROLE OF SURGERY IN SPONTANEOUS INTRACRANIAL HAEMORRHAGE

BY

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A balanced understanding of the diagnosis and treatment at present available for spontaneous intracranial haemorrhage is extremely important, and this paper presents on the one hand our experience and on the other our considered opinion regarding the treatment of this condition. The term "spontaneous intracranial haemorrhage" is used rather than "subarachnoid haemorrhage," as the major portion of the bleeding may be at any site from the subdural space to the ventricle. Apoplexy in the elderly arteriosclerotic, so classical in its clinical manifestations, is not included.

Prognosis

The prognosis in cases treated conservatively has been reviewed many times in the past few years, and there is no doubt that the initial mortality rate is about 50%, rising with recurrent episodes and in older patients. In our assessment our first consideration was a series of 100 consecutive cases managed conservatively by one of us from 1936 until 1951. Conservative care means rest in bed for at least one month, care of the bowels, sedation, and the judicious use of lumbar puncture. In these 100 cases, 53 female and 47 male, there were 43 deaths during the initial period in hospital. Although these 43 deaths occurred at any time up to six weeks after the onset of haemorrhage, one third (14 cases) occurred in the first 24 hours and another third (15 cases) in the second week. Excluding the first day there were only eight deaths in the first week, and six patients died in the second to sixth weeks. Fairly clear evidence of recurrent bleeding was present in half the patients dying during the first and second weeks and in all those dying after the close of the second week. All the 57 survivors have been traced. Eight of them have died from recurrence of intracranial haemorrhage and two others of intercurrent disease. Twenty of them have been left with some permanent neurological disability, although only seven are completely disabled by hemiplegia or intellectual loss. Of the eight late deaths from recurrence only two have been in the disabled group; the other six have occurred in those who had made a complete recovery from the initial haemorrhage. The deaths have occurred after an interval of time up to 12 years from the initial episode. Four died of a single recurrence, but four others of a second, third, or fourth haemorrhage. Before considering the way in which surgical investigation and treatment may improve both the mortality and

the disability rate, we must seek a fairly clear picture of the varying clinical syndromes and pathological findings.

During the first few hours following a haemorrhage, it is clear that certain patients are dying. These are deeply unconscious, with gross changes in the vital signs. Many have a rapidly increasing pulse and respiration rate, and excessive bronchial secretion; often decerebrate rigidity, with the arms and legs held in marked extension and varying areas of the body covered with goose-skin and beads of sweat. They show no response other than a generalized increased rigidity to stimulation. All others must be judged upon the changing signs that occur in the hours immediately after the catastrophe; some are unconscious to varying degree and others never unconscious at all. Headache and neurological disturbance, such as hemiparesis, visual field defects, cranial nerve palsies, or dysphasia, may be present. It is in these hours immediately after the haemorrhage that an assessment of the patient is most important and illuminating. There are those who regain consciousness quickly, who have no evidence of gross neurological disturbance, or rapidly improve. Others are still semiconscious but their condition has remained unchanged over the passage of time, and these are the ones who may recover also. Others, however, begin to show progression of neurological disturbance characterized by increasing drowsiness or coma and pupillary change. It is this group which is developing increasing intracranial pressure and a tentorial pressure cone, the medial portion of the temporal lobe being pushed down between the midbrain and the margin of the tentorium, causing the posterior cerebral artery to press upon the third nerve and bring about the pupillary dilatation and non-reaction to light, as well as disturbing the blood supply and function of the midbrain. Unless urgent surgical treatment is undertaken haemorrhagic infarction of the midbrain will occur with all the signs of impending and inevitable death.

As the hours pass into days so more and more of the patients fall into their obvious categories. We are left with those obviously recovering, those developing evidence of slowly increasing intracranial pressure, and those with varying degrees of unconsciousness or akinetic mutism and disturbance of autonomic function. In any of these patients gross neurological signs other than disturbance of consciousness may be present, but it is when we look to the pathological state that varieties of signs and symptoms fall into their proper perspective and the correct investigation and treatment become clear. It must be understood that at any time there may be a recurrence of haemorrhage of variable severity.

Diagnosis and Diagnostic Procedures

There are certain features in the history and clinical signs which are important, particularly dramatic onset, which in difficult cases may be the only lead to the diagnosis. In those cases in which the bleeding has involved the subarachnoid space there is usually neck-stiffness and a positive Kernig's sign, but the absence of these signs in the early stage does not exclude the presence of a great amount of blood in the subarachnoid space, especially when there is deep unconsciousness. Auscultation of the head, normally so unrewarding, may elicit the presence of a systolic bruit from an angioma. Varieties of neurological signs, and particularly ocular pareses, may be present in many cases, and in some a typical subhyaloid haemorrhage will be observed in the ocular fundus. Ocular pareses when present as isolated signs are likely to be due to an aneurysm in close relation to the nerves, rather than due to a tentorial pressure cone resulting from an intracranial haematoma, and are therefore valuable localizing signs.

In the early stages, particularly if there has been only a mild or premonitory leak of blood into the subarachnoid space, a variety of lower spinal nerve pains may occur; in one of our patients a diagnosis of appendicitis had been made from the lower abdominal pain, rigidity, and vomiting, whilst another developed an obvious crop of herpetic vesicles around the trunk. The patients in whom a haemorrhage occurs almost exclusively into the substance of the brain may have a sudden onset but a rather slower evolution of a syndrome typified by fairly gross neurological disability and increasing headache, somewhat similar to cerebral abscess. Some cases even more insidious in their progression develop signs of considerably increased intracranial tension with papilloedema and drowsiness, resembling a rapidly developing cerebral tumour syndrome.

Lumbar puncture confirms the diagnosis by the finding of blood or xanthochromic fluid. Where the haemorrhage has been essentially intracerebral, blood is usually absent from the cerebrospinal fluid, but it is surprising how rapidly the fluid may alter, showing a rise in leucocytes and protein content. There are cases of intracerebral haemorrhage which may show a relatively normal cerebrospinal fluid at any early stage, whilst a few days later it may be frankly blood-stained although the patient's clinical condition has remained unchanged or has even improved. This is due to the intracerebral clot discharging itself into some part of the cerebrospinal fluid pathways. In an absolutely uncomplicated subarachnoid haemorrhage the cerebrospinal fluid will have returned to normal in about three weeks. Intracranial tension is usually much raised in cases of intracranial haemorrhage, but in intracerebral clot formation, particularly in the elderly, the pressure may be low, as it is in some cases of chronic subdural haematoma. Although in our experience diagnostic lumbar puncture has never been detrimental, it should be performed with caution, particularly in those cases showing evidence of an early tentorial pressure cone.

Angiography

The essence of investigation of spontaneous intracranial haemorrhage is angiography, and until this has been performed, in the majority of cases, the site and the cause of the haemorrhage are both unknown, and definitive surgical treatment cannot be contemplated. We believe, at this stage in our knowledge, that angiography should be performed on all cases of intracranial haemorrhage unless they have considerable arterial hypertension, which we have regarded as a contraindication. This view may be fallacious, as four of these patients have all died of subsequent haemorrhage within a few months.

The need for angiography at present is to obtain further knowledge, particularly of prognosis as well as the planning of treatment. Our usual practice is to perform angiography by the percutaneous insertion of a needle into the common carotid artery under local analgesia, but in a restless or non-cooperative patient general anaesthesia may be necessary. From 10 to 15 ml. of 35% diodone is injected, which gives a clear radiographic picture of the blood vessels. This must be performed on both sides in all cases, with compression of the opposite carotid artery to prove the adequacy of the collateral circulation through the circle of Willis.

Having made such a demand for angiography, it is only right that its possible dangers should be carefully considered. In only one case in which angiography has been performed for the diagnosis of spontaneous intracranial haemorrhage has there been any detrimental result, and this was a mild decrease in the conscious level of a patient who died several weeks later with infarction in the region of the hypothalamus and the anterior portion of the corpus callosum, the angiographic pictures having been thought to be quite normal. In 200 consecutive carotid angiographies performed for a variety of reasons, there has been one death, due to a thrombosis of the internal carotid artery

which was the site of a previous partial occlusion. Seven other patients, all suffering from organic brain disease, have shown some transient increase of physical signs following the investigation. Air studies of the ventricles are necessary only in confirming the presence of an intracranial clot, though ventriculography at a later stage may show a cyst which was a previous clot cavity in communication with the ventricle. The method should be by ventriculography rather than air encephalography, so that the intracranial pressures are disturbed as little as possible to avoid a recurrence of bleeding. An electroencephalogram is a useful adjunct to other investigations in cases of intracranial clot, and also in proving the tolerance of carotid artery occlusion.

Some Outstanding Facts

Using these methods of investigation in 50 consecutive cases referred to us for a variety of reasons and at variable lengths of time after the initial haemorrhage, certain outstanding facts emerge from their comparison with the 100 cases previously referred to in this paper. The first point is that the causes of haemorrhage demonstrated in the living differ from those found in the dead. In all reviews of the natural history of spontaneous intracranial haemorrhage based upon necropsy findings, aneurysm is the greatest cause, but angiographic investigations in the living show a much higher incidence of angiomata. Even after severe haemorrhages, and in some cases where large intracerebral clots exist, no cause can be demonstrated either on angiographic investigation or at operation. This is not surprising, since haemorrhage can occur from minute angiomata of capillary type, and this has been the cause of large intracerebral haemorrhages in two of our cases.

It is also true that aneurysms which are not visible on angiography, because of their small size or the almost complete occlusion of their cavity by clot, may be the cause of severe haemorrhage. In this respect one patient of ours, having a left-sided aneurysm which had given rise to bleeding and a right-sided hemiparesis, died in hospital as a result of haemorrhage from an aneurysm of the right internal carotid bifurcation which could not be seen on angiography four days previously. At necropsy this aneurysm was found to be completely full of clot, and a slit in the arterial wall beside the aneurysm had caused this torrential haemorrhage. The usual finding, however, will either be a typical small aneurysm, an angioma, or, more rarely, a very large saccular aneurysm which may have reached most remarkable dimensions. It is in these large aneurysms that relatively small haemorrhages seem to occur into the aneurysmal wall, producing cranial nerve paralysis by direct involvement of the nerves and large amounts of clot within the sac.

The following table of figures compares the post-mortem findings in the deaths occurring in the 100 cases treated conservatively with the angiographic and operative findings in those treated surgically, and demonstrates the different aetiological factors in the living and the dead.

Cases of Spontaneous Intracranial Haemorrhage

100 Cases Treated Conservatively (43% Initial Mortality)		50 Cases Investigated and Treated Surgically (12% Immediate Mortality)	
Findings at 35 Necropsies		Living	Dead
Aneurysms ..	29 (85%)	29 (58%)	5 (10%)
Angiomata ..	2 (6%)	8 (16%)	0 (0%)
No cause found ..	4 (11%)	11 (22%)	1 (2%)

Angiography may demonstrate the cause of the haemorrhage and also show distortion of the cerebral vessels indicative of intracranial clots.

In several cases we have been surprised to find at operation that upward displacement of the middle cerebral vessels shown on angiography, and suggesting a clot in the temporal lobe, has proved to be due to long-continued local oedema. The findings on investigation may demonstrate the basic pathology, but the vascular anomalies alone cannot always explain neurological disturbances of widespread nature which may occur. Although the angiographic picture of the major arterial tree may appear complete, terminal branches may be affected by either thrombosis or spasm leading to these additional gross and widespread signs. In 3 of the 50 cases surgically investigated no obvious abnormality was found on angiography or ventriculography apart from ventricular dilatation of unknown cause. These patients have all demonstrated a condition of prolonged akinetic mutism and varying autonomic disturbances, and have eventually died. In the two cases in which post-mortem examinations were performed there were small areas of infarction in the medial surfaces of the frontal lobes and hypothalamus, with a tiny aneurysm of the anterior cerebral artery.

Treatment

With all the results of investigations at our disposal four distinct lines of treatment become obvious: non-intervention, to allow natural recovery; evacuation of large intracranial clots; proximal ligation of vessels; and direct attacks upon aneurysm or angioma. Sympathetic interruption is still open to question, but we believe, from the extreme narrowness of vessels often seen on angiography in these cases, that spasm is likely to be present. The aim must be to save the patient's life, make his future more secure, and improve his chances of recovery from severe neurological disability, but in so doing never exposing him to a greater risk. Our investigations have shown such a diversity of gross vascular anomalies, with amazing recovery by natural means alone, that we are sure no one should be exposed to a great risk for an uncertain purpose. Many of these natural recoveries have been so good that they would have delighted the heart of any surgeon who had operated and thought his act responsible for the recovery.

Evacuation of intracranial clots usually means the evacuation of intracerebral ones; the majority of the clot, however, may be in the subdural space, particularly in children. The removal of these clots is not technically difficult; in the acute case it is life-saving, and in the more chronic one it reduces the likelihood of severe persistent disability. These intracerebral clots have certain interesting features: in any particular area the enlargement of clot from the haemorrhage is always along certain apparent well-defined tracks, with the ventricular wall forming the inner boundary. In the very chronic cases the clot is still solid, with a reactive glial wall forming around it, stained yellowish-brown from blood-pigment absorption. Within such a clot cavity will lie the cause of the haemorrhage, and in our experience this is always in one of the walls and not in the centre of the cavity. It is through such clot cavities that aneurysms and angiomata may easily be exposed and local treatment decided upon. In the 35 post-mortem examinations from the 100 cases treated conservatively, 34% had large intracerebral clot formations, and there is no doubt that these clots were the cause of fatality in most of these cases. In the 50 cases surgically managed, 16, or 32%, have had intracerebral clots. All those from whom clots were evacuated survived, but mistaken surgical judgment in three cases resulted in death of the patient with large cerebral clots existing. Cases with oedema simulating clot benefit a great deal from decompression; therefore the distinction is less important than would be theoretically apparent.

We believe that, whenever possible, proximal arterial occlusion should be the first consideration in any case, and that in many it will remain the ideal or only method applicable. Proof of tolerance of carotid occlusion must always be sought by angiography and trial compression before it is utilized as a permanent treatment. The form of proximal arterial occlusion is best considered according to the type of lesion and its situation. Let us first consider varieties of intracranial aneurysm in this respect. For those upon the internal carotid artery or at its bifurcation there is no doubt that ligation of the common carotid artery, followed at an interval by that of the internal itself, is of great value in reducing the intra-arterial pressure at the site of the aneurysm and leading to thrombosis of the aneurysmal cavity. We hope shortly to show by recordings

of the intra-arterial pressure above the point of arterial occlusion that adequacy of anastomotic circulation can be assessed accurately, and certainty or uncertainty of tolerance predicted. For aneurysms upon the anterior cerebral artery, proximal ligation of the anterior cerebral artery itself just beyond its origin is advised. This also applies to the posterior cerebral artery. For the posterior communicating artery temporary carotid ligation should be employed, with direct attack upon the aneurysm itself in chosen cases. This also applies to aneurysms of the middle cerebral artery, though we are still uncertain of the best treatment of aneurysms affecting this essential vessel.

The angiomata of large size, particularly when they are basal or medial in position or bilateral in extent, are often amenable only to treatment by arterial interruption. Here, as in the case of aneurysms, each and every case must be judged on its own merits, its individual anatomy, and its tolerance to arterial interruption. In this respect individual anatomy often causes great surprise: in one of our cases having a large bilateral angioma in the medial surfaces of the frontal lobes angiography showed that the blood supply to the angioma passed through the internal carotid arteries, and that the normal circulation of the brain was via the external carotid and vertebral arteries. This patient tolerated ligation of both internal carotid arteries, but digital compression of both common carotid arteries immediately proved them to be well named as the arteries of sleep, for the patient immediately became unconscious, only to recover within seconds of release of the compression.

It is important to appreciate the individuality of the cerebral circulation and the need for careful proof of tolerance of its interruption. In particular, ligation should not be performed whilst the collateral circulation may be in jeopardy from high intracranial pressure due to intracranial clots, which must be removed by operation before arterial interruption is undertaken. In this respect sympathetic interruption and carbon dioxide inhalation to produce vasodilatation of the cerebral vessels may be useful to improve the cerebral collateral circulation.

The exposure of aneurysms is usually not in itself technically difficult, although it may prove an anxiety to the surgeon and his assistants. The fear of torrential haemorrhage always exists, even though this can be controlled to a large extent by hypotensive drugs and arterial compression. There is really no part of the circle of Willis above the tentorium which cannot be exposed surgically, but, when an aneurysm is found, often only one side of it can be seen so that a number of vessels taking origin from the aneurysmal wall may remain unseen. Carotid interruption will reduce the pressure in aneurysms even of the posterior communicating artery; at operation we have seen fairly large vigorously pulsating aneurysms of this artery cease pulsating, both visually and to a palpating finger, when the carotid artery has been occluded in the neck. If at this stage the aneurysmal wall is opened, blood flows from the aneurysm in a steady stream, which undoubtedly represents the diastolic pressure. The aneurysmal cavity can now be packed with muscle, bleeding controlled, and the cavity completely obliterated. We believe that packing of the aneurysm in appropriate cases is the best treatment, and, failing this, wrapping of the aneurysm in muscle or gauze. The wrapping of an aneurysm is possible only when it is completely exposed, and we have found it to be of considerable value with the small dangerous aneurysms of the middle cerebral artery. Clipping the neck of an aneurysm has not been possible in our hands, and we doubt if by this method the danger area of the aneurysm—namely, the neck and its junction with its parent artery—is rendered safe. It is unfortunate that obliteration of the aneurysmal cavity is no proof that there will not be a torrential haemorrhage from rupture of the artery close to the neck of the aneurysm, which itself is full of organized laminated clot. We must therefore follow up with great care our cases treated surgically, to see if their future is better than that of those treated conservatively.

The removal of a cerebral angioma may be very simple, particularly if it is a small one lying within the wall of a clot cavity or cyst cavity resulting from a previous haemorrhage. On the other hand, a large ramifying angioma may be extremely difficult to remove and the patient's life jeopardized by the attempt. We must remember, therefore, that the natural history of the angiomata is not so menacing to the patient's life as that of aneurysms. These angiomata must be very carefully assessed and the patient's disability considered before removal is decided upon. Certainly it has not been our experience that epileptic attacks can be diminished by the removal of these vascular anomalies.

Surgical treatment as outlined above will undoubtedly reduce the number of deaths due to intracranial haemorrhage of varying cause and severity, particularly those deaths occurring several days after the initial haemorrhage. It is unlikely that the mortality rate over the first 24 hours will be altered very much. It will be remembered that 34% of the cases examined at necropsy in the conservatively treated group had large intracerebral clot formations, and it is true to say that a large percentage of this group could have been saved by surgery. Well-planned proximal ligation will reduce the pressure within the aneurysm and its parent vessels and probably reduce the incidence of recurrent haemorrhage. The incidence of recurrent haemorrhage will also be reduced in those cases in which aneurysms or angiomata are completely removed.

The reduction in the mortality rate inevitably increases the number of patients surviving with a disability, and, whereas in the conservatively treated group 35% of the survivors had residual defects, 52% of the survivors in the surgical group were left with some form of neurological disability. In only 12%, however, was this severe enough to prevent gainful employment, and it was in these six patients that the three late deaths occurred. Disabilities among the survivors from spontaneous intracranial haemorrhages make the need for physiotherapy, speech therapy, and nursing care greater. The provision of facilities for investigation, treatment, and aftercare of these patients is an increasing problem in the neurosurgical departments of the country.

Conclusion

Spontaneous intracranial haemorrhage is a dangerous and treacherous occurrence. The initial catastrophe may be overwhelming, and death may take place in a few minutes or hours; but, should a victim of such a haemorrhage survive beyond this, other dangers no less severe lie before him. Provided the first 24 hours are passed few deaths occur in the first week, whilst in the second week the number of deaths equals that of the first 24 hours, unless surgical investigation and treatment are undertaken. These later deaths are due mainly to large intracranial clots or recurrent haemorrhages. The surgical aim, therefore, should be to investigate these patients in the first week after the initial haemorrhage, so that intracranial clots may be removed or other operative procedures performed to prevent recurrence of haemorrhage. Investigation of spontaneous intracranial haemorrhage is of great importance, for there is no doubt that surgical intervention can improve the individual patient's expectancy of life and reduce his neurological disabilities.

Summary

One hundred cases of spontaneous intracranial haemorrhage treated conservatively have been analysed and compared with 50 cases investigated by angiography and treated surgically. It has been shown from these figures that angiography should be done in the first week following the haemorrhage, so that removal of intracranial clots and the treatment of vascular anomalies by proximal ligation or direct attack may be undertaken in order to prevent recurrence of haemorrhage. It has been stressed that caution is needed not only in treatment but in assessing its curative value. There is no doubt that great help can be given to individual patients and the mortality rate considerably decreased.

REVIEW OF MENTAL ILLNESS IN THE OLDER AGE GROUP

BY

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This review of 198 female patients admitted at the age of 60 or over to one particular section of the Royal Edinburgh Hospital for Nervous and Mental Disorders is designed to call attention to the wide variety of clinical syndromes found in this age group. The choice of the age of 60 as a base-line is deliberate, and is a tacit recognition of the conventional tendency to attribute any gross deviation in thought and conduct observed in patients over 60 to a greater or less degree of "senile" pathological change in the cerebral vessels or brain parenchyma. It may be remarked at the outset that our findings do not corroborate this popular assumption. Many other types of toxi-infective, neoplastic, or degenerative cerebral disease may be the underlying cause. Moreover, while it is wise to look first of all for an organic lesion to explain mental symptoms at this period, it is also true that the so-called "functional" psychoses—notably depression—may erupt for the first time in the individual's life cycle after the age of 60. All these alternatives add to the difficulty of diagnosis, but they also imply that prognosis and reaction to treatment may be better than is usually thought.

In the past ten years many excellent papers have appeared on this subject of mental illness in the older section of the population. The majority of these, however, deal with the statistical implications of the rise in mental morbidity in this group. Only a minority are devoted to clinical aspects. This discrepancy has been emphasized by Professor Aubrey Lewis (1946), who states: "The clinical is probably now the most neglected field in the study of the psychiatry of ageing. . . . I would therefore plead for a greater interest in the straightforward clinical aspects of mental disorder as seen in the aged." Even in the few clinical studies published, clinico-pathological confirmation is sometimes lacking, yet it is precisely in mental illness in the elderly, which is often too readily ascribed to senile degenerative processes, that necropsy studies are most valuable.

Clinical Material

The 198 patients reviewed represent all the female patients of the age of 60 or over admitted to one section of the hospital during the six-year period January 1, 1946, to December 31, 1951. Each patient was studied by one of a group of six physicians, and all were under the observation of one of us (E. E. R.) throughout their stay in hospital in the period under review. The number of admissions of the over-60 group during this period was 244, and the number of individual patients 198. The discrepancy between the two figures illustrates the well-known tendency for affective psychoses to recur; for, apart from a few patients with "arteriosclerotic episodes," nearly every patient with two or more periods in hospital suffered from recurrent manic or depressive episodes. The social background of the patients can be summarized by the statement that they represented a cross-section of all social grades with the exception of the very wealthy.

At the end of the five-year period 81 (41%) had been discharged, 38 (19%) were still in hospital, and 79 (39%) had died. (These figures refer to individual patients.) Thirty-four necropsies were performed, representing 43% of all deaths. This is not as high a necropsy percentage as we could have wished, but every doubtful case was included. This may be illustrated by reference to group II, which included the supposedly rare organic states, such as Alzheimer's disease, Pick's disease, cerebral tumour, etc. In this group necropsy was carried out in every case of death. In addition 14 necropsy reports on patients admitted at the age of 60 or over during an earlier period, but dying in the period under review, were scrutinized for comparison. Of the 14 patients, 10 suffered from an organic cerebral disease and four from a depressive psychosis.

The diagnostic classification of the 198 patients is summarized in the accompanying Table.

Diagnostic Grouping

	Total	Age on Admission		Deaths During Period	% Necropsies to Deaths
		60–69	70+		
A. Unequivocally organic psychoses (total, 92):					
Group I: Cerebral arteriosclerosis and senile dementia	68	9	59	47	30%
Group II: Organic cerebral disease not included in group I:					
(*a*) Alzheimer's disease 10	24	24	—	5	100%
(*b*) Pick's disease 2				1	
(*c*) Cerebral tumour 3				3	
(*d*) Amyotrophic lateral sclerosis with mental symptoms 1				1	
(*e*) Syphilis 3					
(*f*) Drug intoxications 3					
(*g*) CO poisoning—cerebral lesion 1				1	
(*h*) Myxoedema 1					
B. "Functional" Psychoses (total, 96)					
Group III: Affective states:					
(*a*) Uncomplicated: Depression 54, Mania 4	58	51	7	4	
(*b*) Depression secondary to physical disease:					
(i) Extrapyramidal disease 3	7	5	2	6	
(ii) Cardiac disease 2					
(iii) Aortitis 1					
(iv) Carcinoma 1					
	65	56	9	10	40%
Group IV: Paraphrenia and schizophrenia	23	15	8	6	33%
Group V: Psychopathic states	8	8	—	—	
C. Group VI: Mixed organic and affective symptomatology (total, 10)	10	7	3	5	66%

A. Organic Psychoses.—Slightly less than half the total number of patients reviewed (92 out of 198, or 46.5%) suffered from organic psychoses—that is, they displayed intellectual and emotional disturbances of the type found in association with pathologically verifiable lesions within the brain (groups I and II).

B. Functional Psychoses.—The number of patients diagnosed as suffering from one or other of the so-called "functional" psychoses (affective states, schizophrenia, psychopathic states) was roughly similar, being 96 out of the total 198, or 48.4% (groups III, IV, and V). Here the mental disturbance was confined to the emotional sphere and intellectual defects were absent. (We are aware that this differentiation between organic and "functional" psychoses on a

basis of presence or absence of intellectual defects is an over-simplification. The aggregation of mental symptoms seen in frontal lobe tumour or as a sequel to some cases of encephalitis, for instance, may include no intellectual defects measurable as such, yet they none the less warrant the designation of organic psychoses. But, accepting this dichotomy between "emotional" and "intellectual" as artificial, it is nevertheless a useful abbreviation for present purposes, and avoids the necessity for summarizing the other manifold criteria of differentiation between the organic and "functional" psychoses.)

C. In 10 of the 198 patients, or 5%, difficulty was experienced in deciding whether the patient was suffering from a pure affective state—the predominant affect in all 10 was depression—or whether senile organic change coincided. They are accordingly classified under the designation "mixed symptomatology" (group VI).

Age Incidence

Illustrated in Fig. 1 are the relative proportions in each diagnostic group, and also the age incidence. It will be noted that by far the greater number of patients diagnosed

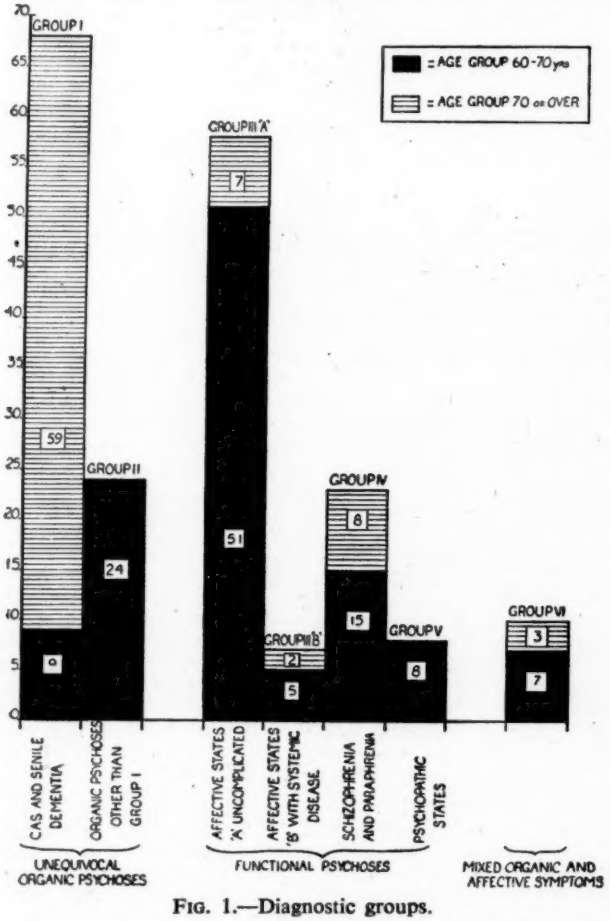

FIG. 1.—Diagnostic groups.

as suffering from cerebral arteriosclerosis and senile dementia (group I) were aged 70 and upwards at the time of admission; only 9 of the 68 were aged 60 to 69. An almost exact reversal of this ratio is found in the second largest numerical group of affective states (groups III, *a* and *b*), where 56 were aged 60 to 69, and only 9 were aged 70 or upwards at the time of admission. Patients suffering from organic cerebral disease other than cerebral arteriosclerosis and senile dementia (group II) were all aged 60 to 69 on admission. The smaller groups IV, V, and VI show a similar preponderance. This suggests that mental symptoms occurring in patients between the ages of 60 and 69 give rise to infinitely more varied diagnostic possibilities than those occurring in later decades.

A. Organic Psychoses (92 Cases)

Group I: Senile Dementia and Cerebral Arteriosclerosis (68 Cases)

Sixty-eight patients—approximately one-third of the total patients reviewed—suffered from cerebral degenerative processes classically associated with old age, and of these only 9 were under 70. Senile dementia (in which degeneration occurs primarily in the parenchyma of the brain) and cerebral arteriosclerosis have been bracketed together, since, despite the dicta of some writers, they are not always easy to differentiate on clinical grounds alone. The slow but relentless mental deterioration, global memory defect, and absence of focal neurological signs seen in senile dementia have been contrasted with the fluctuating course, greater retention of personality, and frequency of focal signs regarded as characteristic of cerebral arteriosclerosis. Admittedly, the typical case of either is easily recognized. For instance, using the accepted criteria of diagnosis of cerebral arteriosclerosis, we readily concluded, on clinical examination alone, that 8 of the 9 cases in the 60 to 69 age group and 15 of the 59 aged 70 or over were suffering from cerebral arteriosclerosis and not senile dementia. But cerebrovascular disease does not invariably present with the triad of signs popularly ascribed to it. When vascular changes occur primarily in the smaller cerebral arteries—a condition which by reason of its specific pathology warrants the separate title of *arteriolosclerosis*, the clinical picture closely simulates that seen in senile dementia. And even *atherosclerosis*, or disease of the larger arteries, particularly when it occurs after the age of 70 and is "decrescent" in type—that is, unaccompanied by peripheral hypertension—may follow a steady unremitting course, more reminiscent of senile dementia than "classical" arteriosclerosis. Another obvious difficulty is that these pathological conditions may appear in combination. In 24 consecutive necropsies the lesion was found to be sufficiently discrete to merit subdivision in 16, which were made up as follows: atherosclerosis 8, arteriolosclerosis 3, and senile dementia 5; while the remaining 8 cases showed varying combinations of parenchymatous and vascular disease. We stress these points deliberately because we have observed that writers demarcate these conditions on clinical grounds alone, and on this dubious basis draw conclusions on their relative frequency. Although we believe that there are many subtle differences in the mental picture to act as pointers in the differentiation of these senile pathological processes, and that it is an obligatory clinical exercise to attempt such differentiation, we are convinced that separation into two arbitrary categories should not be made unless *all* the cases considered have been submitted to necropsy.

Group II: Organic Psychoses other than Senile Dementia and Cerebral Arteriosclerosis (24 Cases)

In this group the underlying cerebral lesion was the result of a variety of causes, including infection, intoxications, and tumour, such as may occur at any period of life, or degenerative processes of the Pick or Alzheimer type, the aetiology of which is as yet unknown, but which characteristically appear between the ages of 40 and 60—that is, in the "presenile" rather than the senile period. The various syndromes are included in the Table and are illustrated in Fig. 2. This group of patients, all of whom were aged 60 to 69 at the time of admission, numbered 24. This figure should be set beside the number of patients admitted in the same age decade with cerebral arteriosclerosis or senile dementia, who totalled only 9. The nature of our material precludes the drawing of too narrow conclusions from these figures, since it is probable that patients with mild or transient defects based on cerebral arteriosclerosis, for instance, may never be admitted to a mental hospital. Nevertheless, they emphasize that many aetiological factors require consideration before a final diagnosis is made on an organic mental picture occurring between the ages 60 to 69.

Infections and intoxications do not on the whole give rise to difficulty in diagnosis, since the history is usually sugges-

tive and the bacteriological findings are often conclusive. But it is rare to find the presenile degenerative states and cerebral tumour diagnosed before admission—they are most commonly presumed to be cases of cerebral arteriosclerosis or senile dementia. The failure to recognize tumour rests in part on the tendency to regard headache, vomiting, and papilloedema as early and invariable symptoms, whereas in patients of this age group they are either late in developing or may never appear at all. But a more frequent cause of non-recognition is the tendency to mistake or disregard

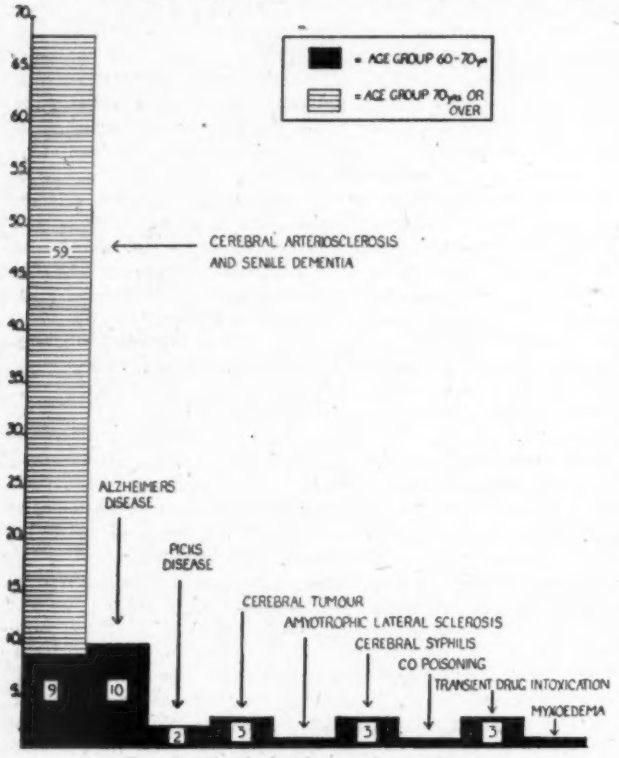

FIG. 2.—Analysis of organic psychoses.

focal signs in the psychic sphere. An aphasic defect in the form of difficulty in naming objects, for instance, may be put down to generalized memory loss. A more severe sensory aphasia may be interpreted as apathy and indolence, or even deafness.

Alzheimer's and Pick's Diseases.—These presenile degenerative diseases accounted for the admission of 12 of the 198 patients reviewed, or approximately 6%. Since they are reported to occur more often in women than in men, a comparable group of male patients might not be expected to show quite the same high incidence. In 10 of the 12 patients, symptoms had appeared before the age of 60. There was reason to believe that the same was true of the remaining two, but their histories could not be adequately ascertained. Necropsy was carried out on all patients who died (Alzheimer's disease, 5; Pick's disease, 1) and the diagnosis confirmed. A long history of steady intellectual decline beginning before the age of 60 should give rise to the suspicion of the existence of one of these presenile degenerative disorders. A remarkable finding in this group is the lengthy duration of the illness before referral for medical opinion—relatives accepting the manifold disabilities of the patient without query. Aphasic and apractic defects are invariably present, and the degree of intellectual deterioration is much more profound than that found in any patient of equivalent age with cerebral arteriosclerosis—unless the latter is accompanied by a severe degree of peripheral hypertension. We believe that Alzheimer's disease and Pick's disease are less rare than is supposed. It is not submitted, of course, that their recognition results in any practical therapeutic advantage to the patient. Nevertheless, at some future date their aetiological elucidation may throw light on general problems of ageing, and, at the present time, statistical surveys of the older hospital patient which neglect the separate diagnosis and classification of this group result in an erroneous interpretation of the frequency of the true senile degenerative states.

B. "Functional" Psychoses (96 Cases)

Incidence of Earlier Mental Illness.—One feature in particular distinguishes the functional psychoses from organic cerebral disease, and that is the frequent finding of earlier mental illness in the former. Such earlier mental illness may have been episodic, as in the affective states, or continuous, as in the majority of cases of schizophrenic or paraphrenic disorder. Or again, as in the psychopathic states, the patient may have shown lifelong aberrations of conduct—such aberrations only on occasion reaching sufficient magnitude to require admission to a mental hospital. In all these cases age may be of little or no importance in aetiology.

Group III: Affective States

Affective psychoses occurring at the age under review customarily take the form of depression—manic reactions are infrequent. This high incidence of depression found in later life has long been recognized by mental hospital physicians. Clouston (1904), in an analysis of cases of "senile insanity," stresses the frequent occurrence of "simple melancholia," adding, "its only special senile character being that it occurred in old people." This phrase admirably describes the cases considered in group III of this series. These also showed the incidental features associated with depression whatever the age of onset, as follows:

1. *High Incidence of Previous Affective Illness.*—All four patients with a manic reaction and 27 of the 54 patients with uncomplicated depression had a history of one or more attacks of a similar illness before the age of 60. All had been capable of normal work in the interval. The remaining 27 of the 54 patients with depression—that is, 50%—had no previous history, and this was also true of no fewer than six of the seven patients who became pathologically depressed in the course of a severe systemic illness.

2. *High Incidence of Attempted Suicide.*—A determined suicidal attempt had been made immediately before admission by 15 of the total group of 65 patients, or 23%. (The methods utilized were: coal-gas poisoning, 6; corrosive poisoning, 2; barbiturate poisoning, 1; cut throat, 2; severed arm vessels, 1; jumping from window, 3.)

3. *Relatively Good Prognosis.*—By December 31, 1951, three of the four patients with a manic reaction had been discharged recovered. Of the 54 patients with uncomplicated depression, 34 (63%) had been discharged recovered. Of these 34 recoveries, however, six had been admitted on two or more occasions during the six-year period with recurrent depressions, and the prognosis in regard to the future of these six was doubtful. This leaves a corrected sustained recovery rate of 28 out of 54 cases of depression, or 52%. Twenty of the 54 did not recover, and, of these, four had been discharged, twelve were in hospital and four had died by the end of the period. Electric convulsion therapy was given to 32 of these 54 patients aged 60 or over. A surprisingly large number recovered in the first month following admission without the aid of E.C.T. A similar observation has been made by Karagulla (1950) in a study carried out in this hospital on a large series of depressions in all age groups. Of the seven patients (group III, *b*) whose depression occurred on a background of severe physical illness, six died as a result of the underlying illness and one was discharged.

4. *Absence of Gross Histopathological Findings in the Brains of Patients Dying During a Depressive Illness.*—The absence of intellectual defects in the clinical picture of these senile depressive states was reflected in a similar absence of gross cerebral pathological change in those cases submitted to post-mortem examination. The histopathological findings in eight cases (four belonging to this series and four relating to similar patients admitted before 1946 but dying in the period under review) in no way differed from those reported in patients dying at the same age period with other than mental disease. Slight gyral atrophy, slight patchy atheroma, or a minor degree of arteriolosclerosis unaccompanied by gliosis or cellular loss were usual findings. Two cases showed no pathological abnormalities.

Relationship of Depressive Psychosis to Ageing.—The finding that 50% of all patients with depression had no history of a similar illness in earlier life—and the additional

finding that in the 50% previously affected long periods of normal functioning had intervened between their former illness and present breakdown, would suggest that the ageing process plays some contributory part in the causation of such depressive illnesses. In this respect depression differs from the other functional psychoses responsible for the admissions of patients in this age group (see below).

Group IV: Schizophrenia and Paraphrenia (23 Cases)

In this group a history of earlier mental illness was obtained in no fewer than 20 of the 23 patients, and in these cases the description given was rarely one of episodic breakdown with intervals of normal functioning as in the foregoing cases of recurring depressions, but took the form of a long-standing socially incapacitating mental illness. In 15 of these 20 the lengthy duration of the illness was confirmed by hospital case records, in 5 by evidence of relatives. Illnesses of 20 to 30 years' duration were common. One patient had first been admitted to this hospital 42 years previously, had been removed a year later, and had lived the life of a recluse under the care of her relatives until her second admission at the age of 68. It was more common to find that these patients had a history of frequent long sojourns in hospital, yet their records also illustrated that a florid schizophrenic thought disorder was not incompatible with equally long periods spent outwith hospital supervision. These are, of course, commonplace facts of mental hospital experience. They are reiterated here in order to stress that admission to hospital with a schizophrenic or paraphrenic illness after the age of 60 does not necessarily imply that the patient first developed symptoms at this age. In only 3 of the 23 patients in this group was the illness of seemingly recent onset. It is appreciated that paranoid symptoms as distinct from paraphrenia are common in this age group. They may occur in depression or in association with organic cerebral disease. But the "systematized delusional insanity" of the older writers would appear from these figures to begin only infrequently after the age of 60.

Group V: Psychopathic States and Epilepsy

These eight patients had shown lifelong aberrations of conduct: in five these aberrations had been so severe as to lead to frequent earlier admissions to a mental hospital. In three the conduct disorder had displayed itself in chronic alcoholism; one suffered from epilepsy, with concomitant emotional disturbance; while the remaining four had displayed antisocial conduct throughout life. This number does not truly indicate the proportion of such patients admitted at the age of 60 or over. Two of the cases of drug intoxications in group II were drug addicts with psychopathic character anomalies. One of the cases of cerebral arteriosclerosis in group I had a long history of behaviour disorder, including chronic alcoholism, and had been admitted at an earlier age with a Korsakoff's psychosis. The necropsy findings in this case revealed, in addition to vascular softenings, an extreme reduction in size of both mamillary bodies—an observation of interest in view of the earlier Korsakoff's psychosis. Nevertheless, if a few such cases with psychopathic character anomalies are added, the total number is still small. This corroborates the accepted hypothesis that age, by diminishing the aggressive urges, ameliorates to some extent the condition of this unfortunate group (Henderson, 1939).

Group VI: Mixed Affective and Organic Symptomatology (10 Cases)

The predominant affect in all these 10 patients was depression—four had made determined suicidal attempts before admission—yet they also showed features suggestive of organic cerebral disease. Only two recovered. Their recovery was rapid; electric convulsion therapy was not given, and afterwards they showed no intellectual defects other than those explicable in terms of normal senility—both were over 70.

The remaining eight formed a homogeneous group, alike in clinical symptomatology and the intractable and distressing nature of the illness. All displayed extreme agitation, perseveration in speech and action, and, finally, profound deterioration in personal habits. Of these eight patients five received one or more courses of convulsion therapy, and prefrontal leucotomy was later performed on one of these five. At the end of the period reviewed, three were still in hospital unchanged and five had died. Necropsy was carried out in three of the five deaths. In the first, macroscopic and microscopical examination of the brain was negative; gyral atrophy and a mild cortical arteriolosclerosis were demonstrated in the second; while in the third a somewhat more severe arteriolosclerosis with slight nerve-cell loss was reported. All three patients were aged 65 to 69 at the time of death. While it would be tempting to postulate of the eight cases showing this malignant syndrome that senile cerebral changes may aggravate and perpetuate a depressive illness, no conclusions can be drawn from these equivocal findings in a small number of necropsies. It may be that, despite the seeming organic nature of part of their symptomatology, these patients actually suffered from a true depression and that the necropsy findings are fortuitous. We feel, however, that their separation from the other cases of depression in this series is justified both by reason of the particular clinical picture shown and because they emphasize the existence of a group of resistant depressions not susceptible to amelioration by physical methods of treatment.

Summary

A review is made of a group of 198 female patients admitted to a mental hospital at the age of 60 and over. Attention is drawn to the diversity of clinical syndromes found.

Approximately one-third of the total suffered from the cerebral degenerative processes commonly associated with old age—namely, cerebral arteriosclerosis and senile dementia. These two conditions are bracketed together, since necropsy studies indicated that they could not always be differentiated on clinical findings alone. One-eighth of the patients suffered from other types of cerebral disease, and this demonstrates that organic dementia occurring in later life should not be too readily ascribed to cerebral arteriosclerosis or senile dementia.

Approximately another third of the total were admitted with a diagnosis of depression. Half of these patients had a history of previous depressive episodes, while half developed a depression for the first time after the age of 60. This suggests that age has some importance as a contributory factor. Two smaller groups of patients were diagnosed as suffering from schizophrenic-paraphrenic psychoses and psychopathic states. The history in almost all these cases revealed that the psychosis or personality anomaly had been manifest long before the age of 60.

All these findings denote that *en bloc* statistics of mental hospital admission can give only inadequate information on the mental sequelae of ageing.

Our thanks are due first of all to Professor Sir David K. Henderson, not merely for permission to publish these cases, but for his teaching, with its emphasis on the importance of exact diagnosis in the organic psychoses. We are indebted to Professor A. M. Drennan and his associates in the neuropathology department, Edinburgh University, for the detailed pathological reports. It is a pleasure to acknowledge the help of former assistant physicians—notably Drs. S. Karagulla, B. Magill, B. Allen, and J. H. Brown—whose careful case histories revivified our memory of the individual patients. The diagrams were drawn by Mrs. N. L. Mason Browne.

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EFFECTS OF TESTOSTERONE IMPLANTS IN MEN WITH DEFECTIVE SPERMATOGENESIS

BY

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The causes of defective spermatogenesis in men are largely unknown, and it will generally be agreed that the methods of treatment, correspondingly empirical, are for the most part ineffective. It has seemed justifiable to try any form of treatment which might help at least some men, and, provided sufficiently accurate data are collected, there is no doubt that trials of this kind are fully warranted. Too often, of course, treatment has been given because a single seminal specimen failed to reach acceptable standards; conclusions drawn from such instances are usually misleading. Consequently, lack of adequately controlled observations in most of the literature dealing with this subject has led to a widespread therapeutic nihilism and its attendant apathy. The prevalence of seminal deficiencies, and our ignorance of how to deal with them, demand, of course, a very different attitude.

There is little doubt that testosterone plays a part in spermatogenesis, though its exact role is still uncertain. There is equal certainty that large doses of testosterone will inhibit spermatogenesis, through its action in depressing the production of pituitary gonadotrophin. Heckel *et al.* (1951, 1952), as is now well known, maintain that on cessation of high-dosage testosterone administration the sperm count rises, not only to its pre-treatment level, but, by reason of a rebound effect, to far higher levels. Other workers have been less impressed by this rebound phenomenon, which is certainly missing from many cases treated according to the method of Heckel. It has seemed possible, on the other hand, that continuous low-dosage testosterone administration might actually stimulate spermatogenesis, or improve sperm motility when this is the deficient characteristic. In order to examine this possibility implants of testosterone have been given to a number of men with various kinds of seminal deficiencies. Implantation was chosen as the route of therapy since it is convenient—a single implant remaining effective for some six months—and affords a slow continuous administration of the steroid.

Material and Methods

The men treated in this series were patients attending the Fertility Clinics at University College Hospital and at the Hospital for Women, Soho Square. Seminal analyses on masturbation specimens were made by a standardized technique, which was the same at both hospitals. They involved determination of volume, density, total percentage of abnormal forms and motility indices according to the method of Emmens (1947) at two or more times. The general plan adopted was to obtain three seminal specimens, each preceded by a three-day (at U.C.H.) or five-day (at Soho) period of abstinence (the difference in period of abstinence seems to be immaterial) before treatment; to administer either two or three 100-mg. pellets of testosterone by subcutaneous implantation at the upper outer aspect of the thigh, just below the iliac crest; and to analyse three further seminal specimens, collected one, two, and three months after implantation. Naturally this plan miscarried on several occasions.

In all, 83 implantations were made in 72 men. Of these, 16 men failed to furnish any post-treatment specimens and so must be discarded. There thus remain for analysis 56 men who received 67 implants. Twenty-eight implantations were of two 100-mg. pellets and 39 were of three 100-mg. pellets of testosterone.

Results

General Effects on Seminal Fluid.—In the first place, the mean figures before treatment for each individual for volume, motility, density, and morphology were compared with the corresponding mean figures after treatment. On this basis, it appears that some degree of general improvement in the seminal fluid was found in 28 individuals, of whom 12 had received 200 mg. and 16 had had 300 mg. of testosterone. In 22 men the findings appeared to be unchanged; while in the remaining six men the post-treatment specimens were definitely worse. In this last group, one man had had 200 mg. and five men 300 mg. of testosterone.

The next step in the analysis was to compare the mean figures for all volumes, motilities, densities, and morphologies before treatment with the corresponding figures after treatment. In dealing with motility it was necessary to find a suitable expression for the comparison of different specimens, the motilities for which might have been recorded at different times after production. For this purpose the "five-hour motility" figure has been used. To calculate this, the motility scores, which range from 4 (maximum) to 0, were plotted against the age of the specimen at the time of scoring, a straight line being drawn through the points. The score at five hours was thus interpolated, and was then expressed as a percentage of the maximum figure 4. Thus, if the interpolated motility index at five hours was found to be 3, the "five-hour motility" would be $\frac{3 \times 100}{4} = 75$.

The overall results are given separately for 200-mg. and 300-mg. implants in Table I. From this it is clear that, in general, both doses had similar effects; that little change in volume was observed; that motility appeared to be improved and density increased; and that the percentage of abnormal forms was slightly increased.

TABLE I.—*Mean Values and Standard Errors*

		Dose of Testosterone	
		2×100 mg.	3×100 mg.
Volume (ml.)	Before implantation	3·49±0·24	3·42±0·16
	After ,,	3·81±0·23	3·21±0·15
5-hour motility*	Before ,,	34·89±4·28	20·55±2·57
	After ,,	47·27±4·77	35·73±3·43
Density (millions per ml.)	Before ,,	32·08±9·20	26·62±2·04
	After ,,	37·31±7·56	40·94±3·39
% abnormal spermatozoa	Before ,,	37·17±1·99	34·44±2·36
	After ,,	43·66±2·09	35·55±1·07

* For explanation see text.

Motility.—Inspection of the data for individual men showed clearly that where the initial motility was of an extremely low order—the mean five-hour motility figure being 5 or less—implantation was followed by no improvement whatever. Since extreme asthenospermia is thus not susceptible to this treatment, it seemed reasonable to exclude such cases and to compare the pre- and post-treatment data for the remainder. This is done in Table II, from which it appears that comparable improvement is found in both the 200-mg. and the 300-mg. series. Reference to Table III, which combines the results for 200-mg. and

TABLE II.—*Effect on Motility, Excluding Cases of Extreme Asthenospermia before Treatment. Mean Values and Standard Errors*

	Dose of Testosterone	
	2×100 mg.	3×100 mg.
Before implantation	41·11±4·61	25·47±2·92
After ,, ...	57·56±4·56	41·67±3·82

300-mg. implants, shows that the difference between the mean pre- and post-treatment motility figures is highly significant (t=4.08, n=258, P<0.01).

TABLE III.—*Overall Effects: Combined Results for 200-mg. and 300-mg. Implants*

		Mean and S.E.	n	t	P
Volume, ml.	Before implantation	3·44±0·13	177	—	—
	After ,,	3·44±0·13	143		
5-hour motility of selected group (Table II)	Before ,,	31·55±2·60	139	4·08	<0·01*
	After ,,	47·68±2·99	119		
Density (millions per ml.)	Before ,,	29·18±3·56	171	2·035	<0·05>0·01†
	After ,,	39·53±3·57	142		
% abnormal spermatozoa	Before ,,	35·44±1·66	155	1·139	>0·05
	After ,,	37·79±0·88	177		

* Highly significant. † Significant.

Density.—The combined mean densities before and after treatment with 200 and 300 mg. are shown in Table III. The difference is significant, though not highly so (t=2.035, n=313, 0.01<P<0.05). However, when the differences between the mean pre- and post-treatment figures are examined for 200 mg. and 300 mg. separately (Table IV)

TABLE IV.—*Effect on Density of 200 mg. and of 300 mg. of Testosterone*

		Mean and S.E.	n	t	P
2×100 mg.	Before implantation	32·08±9·20	62	0·434	0·05
	After ,,	37·31±7·56	55		
3×100 mg.	Before ,,	26·62±2·04	109	3·780	<0·01*
	After ,,	40·94±3·39	87		

* Highly significant.

it becomes apparent that, while for the former the difference is not significant (t=0.434, n=117, P>0.05), for the latter it is highly significant (t=3.780, n=196, P<0.01). One may conclude, therefore, that an implant of 300 mg. is superior to one of 200 mg. in its effect on sperm density.

Volume and Morphology.—It is clear, from Table III, that implantation was without significant effects on the volume of the ejaculate or on the proportion of total spermatozoal abnormalities.

Pregnancies.—The wives of 20 men became pregnant on 22 occasions, all within six months of implantation. Five of these pregnancies ended with an abortion, the incidence thus being 22.75%. This compares with an abortion incidence of 19.1% in a series of 220 pregnancies in women who attended the Fertility Clinic at University College Hospital; an incidence which, it has been shown, is probably not in excess of the general spontaneous abortion rate (Swyer, 1953). Comparison of the mean pre- and post-treatment figures for the individuals whose wives conceived showed an apparent improvement after treatment in 17 cases, no change in 4, and deterioration in 1. These results suggest that conception may indeed have been assisted by the treatment given.

Complications of Treatment.—Testosterone implantation is an innocuous, simple, out-patient procedure which entails no discomfort and does not prevent the man continuing with his work. No patients had any complaints as a result of the implantations, but extrusion of a pellet was encountered on three occasions. This incident is of no serious consequence, and merely requires the application of a dry sterile dressing until the wound has healed.

Discussion

While the statistical analysis of the results of treatment with testosterone implants strongly suggests that motility and density are, in general, improved, inspection of the individual data has made it quite clear that by no means every patient benefited. There can be no doubt that the patients in this series must have presented a very heterogeneous collection of lesions, and it is entirely probable that testicular biopsies before treatment would have shown the unlikelihood of improvement—from any treatment—in many cases. Extreme oligospermia (mean density before treatment 5 millions per ml. or less) and extreme asthenospermia (mean five-hour motility before treatment less than 5) invariably remain unaffected by testosterone implantation. Clearly, the more the series is weighted with unsusceptible cases the less obvious will be the results of treatment; just as if, for example, in attempting to demonstrate the efficiency of penicillin in combating infections the series of cases studied contained a high proportion in which the tubercle bacillus was the infective agent.

Assuming, as appears to be justifiable, that the kind of treatment used here is effective in some cases of defective spermatogenesis, it becomes desirable to determine, so far as possible, which patients are most likely to benefit. It is difficult to lay down hard-and-fast rules, but the following impressions may offer some guidance. As mentioned above, men with extreme oligospermia and extreme asthenospermia (regardless of sperm density) are unsuitable for testosterone implantation. Moderate oligospermia (15–20 millions per ml.) with fair or good sperm activity was improved in 12 cases, remained unchanged in 3, and deteriorated in 3. Poor motility (five-hour motility 15–30) with fair or good density was improved in 14 cases, remained unchanged in 3, but deteriorated in 3 others. These two, then, would seem to be the principal varieties of seminal deficiency for which this treatment might prove of value.

It is suggested as a practical basis that three pre-treatment specimens should be examined, to obtain a fair estimate of the general characteristics of the seminal fluid, and that monthly specimens should be tested for three months after implantation. If these show improvement, but no conception occurs within six months, a further specimen should be examined. If this shows deterioration, a second implantation might be desirable. Obviously, the examination of specimens after implantation is of as much importance to the patient as of interest to the physician, since the decision to use further implants will be governed by the response, if any, to the first one.

In our present state of ignorance, no useful purpose is served by speculating on the *modus operandi* of testosterone in this treatment.

Summary

The effect of implanting two and three 100-mg. pellets of testosterone subcutaneously has been studied in 56 men presenting seminal deficiencies of one kind or another. These men received a total of 67 implants—28 of 200 mg. and 39 of 300 mg. The seminal fluid appeared to improve in 28 individuals (12 received 200 mg., 16 received 300 mg.); to be unchanged in 22 men; and to deteriorate in 6 others (1 received 200 mg., 5 received 300 mg.). No significant overall effects on volume and seminal morphology were seen, but there was a highly significant overall increase in motility with both doses of testosterone and in density with 300-mg. implants. Extreme asthenospermia and extreme oligospermia were invariably unaffected by the treatment.

The wives of 20 of the men became pregnant on 22 occasions, all within six months of implantation; 5 pregnancies ended in abortion (22.75%), the remainder going to term.

It is suggested that moderate depression of sperm density (15–20 millions per ml.) or poor motility (other than extreme asthenospermia) with fair or good density offers the best chances of improvement after testosterone implantation.

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ABDOMINAL TOPOGRAPHY IN RELATION TO SENILE OSTEOPOROSIS OF THE SPINE

BY

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It has been known for many years that there is a tendency to loss of height in late middle and old age (Roberts, 1878). Powys (1901) showed that this loss averages 0.33 in. (0.8 cm.) in every 10 years; the standard deviation of height increases with age, indicating that the rate of decline varies with the individual concerned. Progressive wasting of tissue and the development of senile kyphosis of the spine have been regarded as the main factors involved. As a result of these changes there is an approximation of thoracic cage and pelvis (Brown and Smith, 1945), and in some individuals the costal margin may sink into the cavity of the false pelvis. An extreme example of this deformity is shown in Fig. 1.

FIG. 1.—An extreme example of the deformity produced by descent of the thoracic cage into the cavity of the false pelvis.

The subcostal and supra-iliac lines, traversing the lowest points of the thoracic cage and the highest points of the iliac crest respectively, were originally employed in abdominal topography as the upper and lower boundaries of the umbilical and lumbar regions. Cunningham (1893) showed that these boundaries were unsatisfactory because the distance between them was so variable that in certain individuals the regions so delineated were extremely narrow or even absent. The more widely separated transpyloric and intertubercular lines have now replaced the older boundaries (*Gray's Anatomy*, 1949), but are more difficult to define in routine clinical examination. The approximation of ribs and pelvis in elderly patients results in increased abdominal protuberance and may make detailed palpation of the lumbar regions very difficult. It has even been known to cause acute intestinal obstruction as a result of incarceration of gut between the ribs and the walls of the false pelvis (E. C. Hutchinson, personal communication, 1952).

Previous workers have considered that the main aetiological factor is an increased obliquity of the ribs due to senile kyphosis and muscular weakness, but few accurate observations have been made. The present paper records the results of an investigation of the extent, causation, and possible clinical significance of this anatomical change in the aged.

Methods

Observations were made on 340 subjects (152 male and 188 female). Only adults were studied, and almost all were chronic cases in hospital, with an average length of stay of 2.5 years. This makes the results inapplicable to the general population, the changes due to ageing being probably more extreme in these subjects than in the average. All adult age groups were included, but there were a great many elderly subjects, resulting in a high average age of 68 years. In all cases accurate measurements of the height of the patient and the distance between the subcostal and supra-iliac lines were made. The latter measurement is here termed the "pelvi-costal distance," and the ratio of this to the height of the patient the "pelvi-costal ratio." The convention was adopted of recording these values as negative in the individuals in whom the subcostal line was lower than the supra-iliac line, this extreme deformity being found in only four patients.

As the investigation was designed to study the causation and significance of a low, zero, or negative pelvi-costal ratio, all individuals with a value of this ratio below 1% were subjected to full radiological examination of the lumbar and dorsal spine. This sample consisted of 22 males and 32 females, and, as expected, contained a disproportionate number of elderly patients, the average age being 74. A group for comparison was taken from the remaining 286 patients. This group was selected to contain exactly the same number of males and females as the previous group and to have precisely the same age distribution, the method of random numbers being employed in choosing between suitable individuals. It follows, therefore, that the two groups were exactly comparable except that the former consisted only of individuals with an abnormally low pelvi-costal ratio and the latter with an average ratio for the age group concerned. These two groups will subsequently be referred to as the "cases" and the "controls."

The following measurements were considered to be possible factors in the production of an abnormally low pelvi-costal ratio, and were obtained directly from the *x*-ray plates: (*a*) the angle between the lower ribs and the anterior border of the lower dorsal spine; (*b*) the degree of lumbar lordosis expressed as an angular measurement; (*c*) the length of the lumbar spine; (*d*) the proportion of the lumbar spine occupied by the intervertebral disks; and (*e*) the degree of spinal osteoporosis.

The last factor is very difficult to express in a quantitative manner, as has been well discussed by Lachmann and Whelan (1936). It was thought impossible to assess the degree of osteoporosis directly from the radiological density of the vertebral bodies, since this is partly dependent on factors which are difficult to control, particularly the exact photographic exposure and the radiological density of soft tissue superimposed on the vertebral shadow. The effect of osteoporosis on the shape of the vertebral body—that is, the production of biconcave or "fish-" vertebrae—was therefore chosen as the index of its degree. The most accurately centred lumbar and dorsal vertebrae were chosen in the lateral films, and the heights of the anterior and posterior borders and the minimum height near the centre of the vertebra were measured. The amount of biconcavity was expressed as the ratio of the minimum height to the average of the anterior and posterior heights, this ratio diminishing with increasing osteoporosis. An assessment of a single accurately centred vertebra was necessary, since parallactic effects make similar measurements erroneous in other vertebrae. In practice there was no difficulty in

deciding which vertebrae were the best-centred, and, with the particular radiological technique employed, these were the eighth or ninth dorsal and the third or fourth lumbar vertebrae in the two lateral films used.

Finally, the length of stay in hospital was recorded as an estimate of the degree of immobilization. Although the great majority of the patients were not confined to bed, their activity in hospital was much less than would be likely in similar individuals in their own homes. Standard statistical methods (Snedecor, 1946) were employed in the analysis of the results.

Results

A preliminary inspection of the means of the pelvi-costal ratios of patients classified in decennial age groups (Table I) showed that there was a sudden decrease in the seventh decade. In order to decide whether the decrease of this

TABLE I

Age Group	Males		Females	
	No. of Patients	Mean Value of Pelvi-costal Ratio	No. of Patients	Mean Value of Pelvi-costal Ratio
<41	13	1·9%	7	2·4%
41–50	10	1·9%	22	2·5%
51–60	18	2·2%	24	2·6%
61–70	33	1·7%	32	1·8%
71–80	49	1·6%	52	1·8%
81–90	28	1·6%	49	1·7%
>90	1	—	2	1·7%
Total	152	1·75%	188	2·0%

TABLE II

Sex	Age Group	Mean Value of Pelvi-costal Ratio	Difference	Degrees of Freedom	t Value	P
Males	Below 65	2·04%	0·43	51	3·2	<0·01
	Above 65	1·61%		99		
Females	Below 65	2·47%	0·76	64	4·5	<0·001
	Above 65	1·71%		122		

ratio with age was statistically significant, patients below the age of 65 were compared with those above this age (Table II). It will be seen that the difference between these two age groups is highly significant in both sexes. The results are summarized in the distribution curves in Fig. 2. The distribution in females has a larger mean and scatter and is more skewed than in males owing to the comparatively large number of individuals with a high ratio in the former sex. This may possibly be connected with the greater lumbar lordosis of the female, but there were too few *x*-ray films taken of individuals with a high pelvi-costal ratio to assess this aspect of the problem. Relevant statistical values of the distribution curves in the two sexes are given in Table III. The curve in males does not differ significantly from a normal distribution, while that for females is clearly skewed, so that the modal value is much less than the mean.

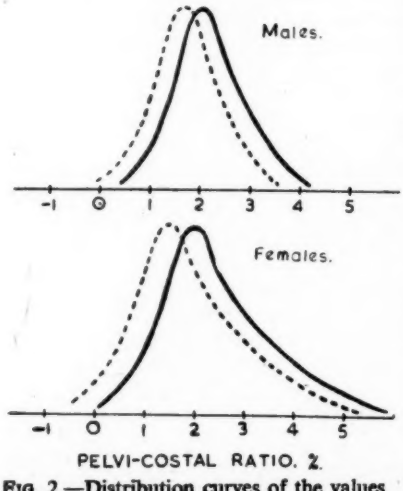

FIG. 2.—Distribution curves of the values of the pelvi-costal ratio in male and female patients. Continuous line = under the age of 65. Broken line = over the age of 65.

TABLE III

Sex	Mean Value of Pelvi-costal Ratio	Standard Deviation	Skewness		
			Statistic g_1	t Value	Probability
Male ..	1·75%	0·87	0·2	1·0	0·4>P>0·3
Female ..	2·0%	1·17	0·5	2·8	P<0·01

Although the "t test" is not strictly applicable to such a skewed distribution, it was shown to be valid by repeating the test with derived logarithmic values of the pelvi-costal ratio, which gave a strictly normal distribution. A similar t value and probability was thereby obtained.

In the comparison of radiographs of the cases having an abnormally low pelvi-costal ratio with those of the controls no significant difference was found in the lengths of the lumbar spines, in the amount of lumbar lordosis, or in the thickness of intervertebral disks. There was, however, a clear difference in the obliquity of the ribs in the two groups. In both sexes the ribs of the cases were on an average 7.5 degrees further from the horizontal plane than those of the controls (t value = 2.8 ; P <0.01).

There was a significantly greater degree of osteoporosis as measured by biconcavity of lumbar vertebrae in the cases. A summary of the statistical analysis of this comparison is given in Table IV. The difference was more striking in

TABLE IV

Portion of Spine	Samples of Patients	Mean of Index of Biconcavity %	Difference	t Value	Probability
Dorsal	Cases	79·7	2·5	1·6	P=0·1
	Controls	82·2			
Lumbar	Cases	69·8	6·4	3·2	P<0·01
	Controls	76·2			

females, eleven of whom were found to have a degree of lumbar osteoporosis of severity sufficient to give an index of biconcavity of less than 67%. All of these were in the group of cases and none in the controls. A comparison of the measurements of the dorsal vertebrae shows a similar tendency, but the difference is not quite significant at the conventional one-in-twenty degree of probability. There was striking biconcavity of vertebrae in most of the spines, the average ratio of the central height to the mean of the anterior and posterior heights of the lumbar vertebrae examined being 73%. This result is almost certainly inapplicable to a healthy elderly population, being an indication of the tendency of patients with long-term illness to develop osteoporosis as a result of relative immobility. In six of the patients examined by radiology the pathological process had progressed further and caused actual collapse of one or more vertebral bodies, almost invariably in the upper lumbar or lower dorsal regions, this being the usual location for this complication (Fairbank, 1951). Three of these were in the group of cases and three in the controls. In almost all the patients the cause of the "fish-vertebrae" appeared to be uncomplicated senile osteoporosis, but in two patients there was Paget's disease with a superimposed osteoporosis ; in a third the characteristic changes of ankylosing spondylitis were found ; and in the youngest individual amongst the cases osteomalacia secondary to idiopathic steatorrhoea was shown to be the cause.

Rather paradoxically, no correlation was found between the degree of biconcavity of vertebrae and the age of the patients. This is probably explained by the fact that almost all the patients examined radiologically were over the age of 65 and that a maximum change is reached at an earlier age in long-term invalids than in the healthy population. There was only a slight correlation between length of stay as an in-patient and degree of osteoporosis (r = +0.20), and this did not differ significantly from zero correlation. It was, however, realized that length of stay was a very poor

estimate of immobilization; but it was the best available in elderly patients usually incapable of giving a satisfactory account of their activity prior to admission.

Discussion and Summary

The results demonstrate that there is a tendency to approximation of the thoracic cage and pelvis with increasing age. The most important factor involved is an increased obliquity of the ribs, which is, at least in part, secondary to the development of senile kyphosis. Radiological evidence of senile osteoporosis is more likely to be found in individuals in whom this change is greater than the average. The explanation may be that osteoporotic shortening of the spine is a further factor in causing this approximation, but, alternatively, it is possible that the rather asthenic type of elderly individual, in whom obliquity of the ribs is above the average, is constitutionally more liable to develop senile osteoporosis.

Senile osteoporosis of the spine is shown to be very common in elderly chronic invalids; indeed, some degree of osteoporosis is almost universal. As in so many other medical conditions, however, it is impossible to define any sharp boundary between the normal ageing process in the spine and pathological osteoporotic change. There is a gradual and continuous variation between spines which, at one extreme, can be regarded as normal for the age group, and those at the other extreme which show severe unequivocal pathological osteoporosis.

From a practical clinical point of view, it can be stated that there is a fair likelihood that spinal osteoporosis of significant degree will be found in elderly individuals in whom the distance between the subcostal and supra-iliac lines is less than 1% of the patient's height, corresponding in most cases to a distance of ½ in. (1.3 cm.) or less.

We are indebted to Mr. K. Bray for carrying out the radiography and to Miss Perry for the clinical photograph.

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The third annual report of the British Empire Society for the Blind was published last week. Preliminary surveys have shown that more than a million people in the Colonies are blind, millions more have incapacitating eye diseases, and facilities are gravely inadequate. Most probably, according to the report, three-quarters of this blindness is preventable. The report describes the start of a systematic attack on "river blindness" (a variety of filariasis affecting the eyes) in West Africa. The disease is spread by a simulium fly. At least 100,000 people in the northern Gold Coast are victims of the disease, which in the past has depopulated whole villages. The Society has sent two teams, one medical under Dr. F. Rodger, an ophthalmologist, and the other composed of entomologists, to survey the problem in the Gold Coast, the Cameroons, and Northern Nigeria. One of the objects of the survey is to obtain exact information on the life history of the vector fly. In East Africa, where conditions are rather easier, treatment of the rivers with insecticides has been followed by a notable reduction in river blindness. Trachoma is another very important cause of blindness, and a pilot survey at Aden last year showed that in some villages everyone had it in some form or another.

ACTINOMYCOSIS IN SCOTLAND

BY

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Since 1891, when Wolff and Israel first isolated the causative organism of actinomycosis, *Actinomyces israeli*, much has been written on many aspects of this disease, but the literature reveals little information regarding its incidence. It is not surprising, therefore, to find in one textbook the statement that it is "not a common disease" (Topley and Wilson, 1946), and in another that it is "not infrequent" (Christian, 1947).

Most people will agree with Cope (1949) that "we must put aside the traditional and popular fairy-tale about infection from grass and straw," since from these sources aerobic actinomycetes only have been isolated. It is now commonly held that the infection is endogenous, arising from the micro-aerophilic actinomycetes found in the human mouth, which resemble closely the pathogenic *Actinomyces israeli*. Associated with the exogenous theory of infection was the suspicion that agricultural workers were more often the victims of this disease than those in non-agricultural occupations. Although our ideas regarding the origin of the infection may have changed, it does not necessarily follow that our views concerning the occupational incidence of the disease must also alter. The question of whether agricultural workers are in fact more prone to actinomycosis than others has not so far been satisfactorily answered. Before it can be it is necessary to relate the number of cases of the disease occurring in agricultural and non-agricultural workers to the total number of individuals at risk in the two groups in the area under consideration. A survey of actinomycosis in the north-east of Scotland in which particular attention was paid to this point has already been recorded (Porter, 1951). In view of the fact that the north-east of Scotland is predominantly agricultural it has seemed desirable to extend this survey to the rest of Scotland, in which there is a large industrial belt in addition to agricultural areas.

Investigation

The extended survey was designed to cover all cases of actinomycosis admitted to hospital for treatment during the thirteen years from 1936 to 1948 in those parts of Scotland not originally reported upon—that is, in the whole of the country excluding the five counties in the north-east. Information was sought from all general hospitals and from *x*-ray therapy departments. Not all the hospitals were able to provide the desired information, sometimes because of inadequate case records and sometimes on account of the absence of comprehensive filing systems covering the period under review.

It is recognized that a number of patients with actinomycosis in its less acute forms may have been treated at home by their own physicians and received no hospital treatment. Such are not included in the survey, and no systematic search of the records of the out-patient departments of the various hospitals was attempted. A few out-patient cases of the disease which had been referred to *x*-ray therapy departments for treatment were obtained from the records of these departments, and these have been included.

Any case lacking bacteriological or pathological confirmation of the clinical diagnosis has been excluded; likewise, a few cases whose normal residence was not in Scotland.

Results

The results of this investigation have been combined with those of the previous survey of the north-east area in order to give an overall survey of actinomycosis in Scotland. Where necessary, figures for each of the surveys are given separately so that they may be compared.

The total number of cases for the whole of Scotland was 186, of which 98 came from the north-east area and the remaining 88 from the rest of Scotland. In view of the fact that at the 1931 Census the population of the five north-east counties (Aberdeen, Kincardine, Banff, Moray, and Nairn) was 444,000, compared with 4,398,000 for the rest of Scotland, it is surprising that the north-east area should account for more than half the total number of cases recorded. Even if allowance is made for the fact that 15.8% of the hospital beds in the rest of Scotland were not covered, there would still appear to be a disproportionately large number of cases from the north-east area.

Location

In a report from the Netherlands, van der Hoeden (1939) stated that actinomycosis was ten times as common in rural districts as it was in large towns. The 186 cases of actinomycosis in this survey were grouped according to whether these patients lived in large towns or not. Thirteen cases had occurred in members of the armed Forces, and, owing to the uncertainty of their location prior to admission to hospital they have been excluded, leaving 173 cases for consideration. The results show that there was no significant difference in the rate of attack between those resident in the large towns and those in the small towns and rural districts in the north-east area. However, when the rest of Scotland is considered it appears that there is a significant difference between the attack rate among residents of large towns and that among residents in smaller towns and rural districts: the disease is more prevalent in the latter group.

Age Incidence and Sex

The ages of 184 of the 186 cases are known, and their distribution in the various age groups is shown in the Chart. The maximum number of cases occurred in the 20–29 age group. The combined number of cases in the 10–19 and 20–29 age groups is 94—just over half the total number. The percentage of the population in each age group is marked on the chart, and it can be seen that in the 10–19 and 20–29 age groups more cases of actinomycosis have occurred than would have been expected from the numbers of the population in these age groups.

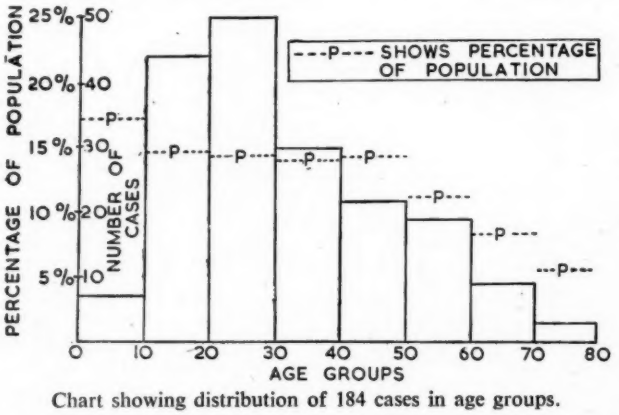

Chart showing distribution of 184 cases in age groups.

Males are more commonly affected than females, as borne out by the fact that of the 186 cases 145 (78%) were males.

Anatomical Distribution and Incidence of Trauma

The cervico-facial region is the most commonly affected portion of the body (65%), followed by the abdominal region, which accounted for 19% of the infections. Actinomycosis of the cervico-facial region had occurred after dental extractions on 22 occasions, and in a further 33 patients in whom carious teeth had been noted. There was a history of injury to the face in 5 cases. In 23 of the abdominal cases there was a history of an associated appendicectomy, and in 2 cases of an appendix abscess. It is commonly agreed that actinomycosis may follow or be associated with appendicitis. Two cases of abdominal actinomycosis followed gastric perforations, and in 3 cases a blow to the chest or abdomen had preceded the onset of the disease.

Occupational Incidence

The occupations of 173 of the 186 cases are known. The occupation which accounted for the largest number of cases was agriculture, which gave a total of 39, two of which were under 16 years of age. Since opinion in the past has been divided on the question of whether agricultural workers are more liable to this disease than those in non-agricultural occupations, it was thought desirable to submit the figures resulting from this survey to statistical analysis. The numbers of those engaged in agriculture and in non-agricultural occupations in Scotland between 1936 and 1948 were obtained through the courtesy of the Ministry of Labour. Only males between the ages of 18 and 64, of which there were 88, were subjected to this analysis. The probability was calculated, and showed that, in Scotland, males between the ages of 18 and 64 engaged in agriculture were more liable to develop actinomycosis than those in non-agricultural occupations. The attack rate for male agricultural and non-agricultural workers in the two areas of Scotland are given in the accompanying Table.

Table Showing Attack Rate of Actinomycosis in Scotland of Male Workers

	North-east Area		Rest of Scotland		Total	
	Cases / O.M.	Ratio per 100,000	Cases / O.M.	Ratio per 100,000	Cases / O.M.	Ratio per 100,000
Agricultural workers	19 / 13,000	146	18 / 62,000	29	37 / 75,000	50
Non-agricultural workers	20 / 61,000	33	31 / 919,000	3·3	51 / 980,000	5·2

O.M. = Occupied males.

Discussion

Our knowledge of actinomycosis has increased greatly during the last 60 years, but there are still many questions to which answers are required. The theory of endogenous infection is now accepted by most workers in this field. *Actinomyces israeli* has been isolated, in the absence of clinical actinomycosis, from carious cavities, from periodontal abscesses, from dental deposits, and from tonsils. Its existence in the mouth offers a possible explanation of the frequency with which the cervico-facial region and the gastro-intestinal tract are affected. It would appear from investigations concerned with the isolation of micro-aerophilic actinomycetes from the mouth that these organisms have been recovered in only some 5% of instances. Thus Lord and Trevett (1936) isolated four strains of anaerobic actinomycetes from dental scum and carious teeth of 90 patients, while Sullivan and Goldsworthy (1940) isolated five strains of anaerobic actinomycetes from 100 periodontal abscesses and one strain from 24 carious teeth. However, Emmons (1937) isolated micro-aerophilic actinomycetes in 23% of cultures from 100 pairs of tonsils.

No details are given of the sex and age of the patients mentioned in these investigations. In view of the fact that this disease is more common in males and in those in certain age groups, it would be of much interest to know if micro-aerophilic actinomycetes are present more often in male than in female mouths, and in certain age groups more often than in others; also if mouths of agricultural workers and rural residents harbour this organism more commonly

than mouths of non-agricultural workers and residents of the larger towns. Such information might be helpful in revealing factors which have so far not been taken into account in working out the epidemiology of this disease.

Although it has been found that male agricultural workers are more liable to actinomycosis than male workers in non-agricultural occupations it does not mean that we must connect this disease with the aerobic actinomycetes found in grains or grasses or even with the presence of the anaerobic *Actinomyces bovis* of lumpy jaw in cattle. Erikson (1940) made a detailed study of 20 strains of micro-aerophilic actinomycetes, 15 of which were of human origin and 5 of bovine origin. She showed that there were certain morphological, physiological, and serological differences between the human and bovine strains. Slack *et al.* (1951), however, in an examination of 11 human strains and 5 bovine strains isolated from cases of actinomycosis showed that they were serologically related. There is little information available concerning the frequency of actinomycosis in cattle and no evidence as yet to warrant connecting bovine with human cases of the disease. The lack of knowledge of the epidemiology of the disease in cattle would appear to be as great as it is in the case of the human subject.

Summary

A survey of the occurrence of actinomycosis in Scotland during the 13 years from 1936 to 1948 revealed 186 cases. All had bacteriological or pathological confirmation of the clinical diagnosis.

The commonest site of infection was the cervico-facial region, and males were more often affected than females.

Male agricultural workers were found to be more liable to this disease than those in other occupations. There was no significant difference in the attack rate of the residents of the larger towns and rural areas in the north-east of Scotland, but the residents of the larger towns in the rest of Scotland were found to be much less frequently the subjects of this disease than those living in essentially rural areas.

I wish to thank the medical superintendents of the various hospitals in Scotland and their records staff for help in obtaining the information on which this paper is based. For advice and assistance on statistics I am grateful to Mr. H. Campbell, Nuffield Department of Industrial Health, King's College, Newcastle-upon-Tyne.

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The City Council of Nottingham has recently published an attractive handbook describing the facilities available in the city for users of the National Health Service. The book opens with a brief summary of the medical services during the last hundred years up till 1948. It then describes in simple terms what maternal and child welfare facilities there are in Nottingham, and gives a detailed account of the work of the health visitors, midwives, district nurses, and home helps. In a chapter entitled "Care Service" the book tells of the services for the prevention of illness, by immunization and vaccination, and the control of the spread of tuberculosis and other infectious diseases. There is also a short description of the sanitary services and of the council's efforts to promote smoke abatement and slum clearance. The handbook concludes with the addresses of hospitals and clinics in and around Nottingham where different kinds of treatment may be obtained.

SPECIFIC BACTERIOLYSIN IN SUBACUTE BACTERIAL ENDOCARDITIS CAUSED BY A HAEMOLYTIC STAPHYLOCOCCUS ALBUS

BY

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This report records a case of subacute bacterial endocarditis (S.B.E.) in which there was serological evidence that the causal organism was a haemolytic coagulase-negative strain of *Staphylococcus albus*. So far as can be ascertained, serological evidence of infection in S.B.E. has not been recorded previously. The particular interest in this case was the presence of a specific bacteriolysin in the serum.

Between 1945 and 1952 British and American literature recorded over 30 cases of S.B.E. due to coagulase-negative white staphylococci, and it has been suggested (Dowling *et al.*, 1952) that this type of endocarditis may be increasing in frequency. Out of a total of 2,100 cases of S.B.E. reported in five reviews (Thayer, 1931 ; Perry, 1936 ; White *et al.*, 1945 ; Priest *et al.*, 1947 ; Cates and Christie, 1951), *Staph. albus* was the causal organism in 20 instances—that is, about 1%. Individual cases are reported from time to time (for example, Cunliffe *et al.*, 1943 ; Matthew, 1951 ; Cobb, 1952), and serve to emphasize the fact that *Staph. albus* should not be regarded invariably as a contaminant when found in the blood cultures from these cases.

Case Report

The patient, a married woman aged 33, had a long "rheumatic" history, having had three attacks of acute rheumatism at 14, 27, and 29 years. Between 1947 and 1950 she was admitted to hospital on four occasions, suffering from various degrees of cardiac failure, with mitral stenosis and fibrillation. In 1947 and 1948 she was in hospital for some weeks; rapid improvement was brought about with rest and digoxin therapy.

On April 13, 1949, she was admitted to hospital for the third time, again with severe fibrillation; as before, this was treated with digoxin. Improvement was rapid, but on May 9 it was found that the spleen was enlarged to one and a half fingerbreadths below the costal margin. A persistent anaemia (Hb, 7 g.%), very marked clubbing of the fingers, and prominent nodules over the elbows were also found. It was thought possible that an early subacute bacterial endocarditis was present, despite the fact that the patient was apyrexial, and a series of blood cultures gave the following results:—May 10: a few colonies of a haemolytic coagulase-negative *Staph. albus*; May 12: no growth; May 16 and 17: a heavy growth of a haemolytic coagulase-negative *Staph. albus*.

In vitro tests showed that the organisms isolated (presumably all the same strain) were sensitive to penicillin; 1,000,000 units of penicillin daily was given when the second positive culture was reported—this was continued for five weeks. The patient's condition improved dramatically with penicillin therapy. The haemoglobin rose to 11.9 g.%, her weight increased, and symptoms of tiredness and malaise disappeared. Nine blood cultures taken between May 25 and July 30 were sterile. She was discharged on August 20.

For some months she continued well, but in February, 1950, she was readmitted to hospital with severe decompensation. During the next few weeks her condition gradually worsened; blood cultures were sterile. Gross cardiac failure developed on May 15, 1950, and death occurred the next day. Permission for necropsy was refused.

Bacteriology

When the staphylococcus was first isolated (May 10, 1950) it was thought to be a skin contaminant, as it is generally accepted that most albus strains isolated from blood cultures fall into this category. The striking feature of the organism, however, was the degree of haemolysis produced on blood agar; the zone of clearing round each colony was almost as great as that found with a haemolytic streptococcus. In other respects the organism appeared to be an ordinary albus strain; the coagulase test was negative. When similar organisms were isolated from further blood cultures (May 16 and 17) contamination seemed unlikely, and the patient's serum was investigated for antibody content.

The results of the various tests showed that the serum did not contain any agglutinins but that a bacteriolysin was present. This bacteriolysin was evidently specific for the staphylococcus isolated from the blood cultures (see Table).

Bacteriolytic Effect of the Patient's Serum on a Range of Organisms

Organism	Serum Dilutions—Reciprocals										
	2	5	8	10	20	40	100	200	500	750	C
Staph. albus A ..	+	+	+	+	+	+	+	+	±	−	−
,, ,, B ..	+	+	+	+	+	+	+	+	−	−	−
,, ,, C ..	+	+	+	+	+	+	+	+	+	−	−
,, ,, 1 ..	−	−	−	−	−	−	−	−	−	−	−
,, ,, 2 ..	+	±	−	−	−	−	−	−	−	−	−
,, ,, 3 ..	−	−	−	−	−	−	−	−	−	−	−
,, ,, 4 ..	−	−	−	−	−	−	−	−	−	−	−
Staph. aureus Oxford	+	−	−	−	−	−	−	−	−	−	−
Str. pyogenes ..	−	−	−	−	−	−	−	−	−	−	−
,, *viridans* ..	−	−	−	−	−	−	−	−	−	−	−
Bact. coli	−	−	−	−	−	−	−	−	−	−	−
B. friedländeri ..	−	−	−	−	−	−	−	−	−	−	−

Staph. albus A, B, and C = the organisms isolated from the three positive blood cultures.
Staph. albus 1, 2, 3, and 4 = four strains isolated from other patients' blood cultures and classed as contaminants. All non-haemolytic.
+ = Clearing of the suspension. − = No change. ± = Partial clearing.

Similar tests were carried out with sera from 12 other patients, including two known cases of S.B.E. due to *Streptococcus viridans*, with negative results. The bacteriolysin was still present in the patient's serum several weeks later, but the lytic titre had fallen to 1:4 within three months. The haemolytic activity of the organism gradually diminished after several months' storage on Dorset's egg medium, and had almost disappeared when examined three years after isolation.

Comment

The anaemia in this case was no doubt due to the haemolytic activity of the staphylococcus: the occurrence of a haemolytic strain of *Staph. albus* in S.B.E. has been noted previously by Allen and Riecker (1949). The development of specific bacteriolysin does not appear to have been reported in other similar cases, and may be a purely isolated finding. Absence of post-mortem data makes it difficult to assess the effect of the septicaemia on the course of the patient's illness, but the degree of cardiac damage was so great that it is feasible to assume that early death was inevitable, irrespective of the blood infection.

We wish to thank Dr. E. Oastler, in whose wards this case occurred, for permission to make use of clinical notes.

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Medical Memorandum

Amoeboma of the Caecum

A male clerk aged 34 was admitted to hospital on November 20, 1949, with a three-days history of right-sided abdominal pain.

On examination he had a normal temperature and pulse, there was a tender mass palpable in the right iliac fossa, and the white blood cell count was 11,000. The case was thought to be an appendix abscess, and was treated with antibiotics. As there was no diminution of the mass after twenty days, an exploratory operation was performed.

Operation.—On December 9 a Rutherford Morison incision was made and a firm, rather inflamed mass was found occupying the caecum and ascending colon. This was thought to be a neoplasm or a non-specific granuloma, and the affected bowel was exteriorized after suturing the ileum to the transverse colon preparatory to a double-barrelled colostomy. Three days later the affected loop was removed and the intervening spur was crushed soon after. Within three weeks there was considerable excoriation of skin around the colostomy, and this rapidly developed into spreading infection with sloughing of the abdominal wall, which increased steadily until *Entamoeba histolytica* was identified in the skin edge and appropriate treatment given.

The condition improved gradually and sloughs separated, but a large granulating area resulted with a faecal fistula in the middle of it. Closure was effected after the third attempt some eight and a half months from the original operation. Tantalum mesh proved useful in bridging the gap in the abdominal musculature, and the skin defect was made good by sliding and grafting. Bowel action has been regular and normal ever since, but two small sinuses developed which discharged sero-sanguineous fluid but no faeces. Part of the mesh had been extruded and cut off, but it was thought best not to interfere further.

When last seen the patient was enjoying excellent health and going to business as usual.

Comment

This case illustrates the importance of excluding amoebiasis when doubtful masses are found in the bowel, especially in view of the relatively large number of persons who have been abroad in recent years. Amoebic ulceration of the abdominal wall seems to be more frequent in the United States—often coming on after appendicectomy in an infected case (Hunter, 1951). Hawe (1945) writes on the surgical aspects of intestinal amoebiasis, and refers particularly to the need of excluding acute caecal amoebiasis before operation for appendicitis in endemic areas. Donald (1940) describes two cases simulating carcinoma of the rectum. It would seem that the cases most likely to cause confusion in endemic areas are those of acute caecal or appendiceal amoebiasis, while the presence of unusual masses in the rectum or elsewhere in the bowel may call for a search for *E. histolytica* in the stools before proceeding to surgery.

Acknowledgments are due to my colleagues at Ashford Hospital, Middlesex, particularly Dr. K. D. Keele, for advice on treatment, and to Drs. W. J. Hamilton and C. F. Ross for pathological reports.

Epsom. E. N. CALLUM, F.R.C.S.Ed.

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Reviews

WILLIAM CHESELDEN

William Cheselden, 1688–1752. By Sir Zachary Cope, M.D., M.S., F.R.C.S. (Pp. 112; 20 figures. £1.) Edinburgh and London: E. and S. Livingstone. 1953.

Although William Cheselden is still, after 200 years, accounted one of the major glories of St. Thomas's Hospital, this volume, written by a consulting surgeon to St. Mary's Hospital, appears to be the first fully documented life to have been published. The author's 1952 Vicary Lecture is the basis, to which he has added much new material resulting from his original researches.

Little is known of Cheselden's early life. Born in the year of the "Glorious Revolution," he lived through the Augustan period of our history, dying in 1752 acknowledged by all (as the *D.N.B.* states) to be the leading surgeon of his age.

For some years before his election to the staff of St. Thomas's Cheselden had conducted regular anatomy classes, which were so successful as to become a necessity for London medical students to attend. He was the first man in this country who insisted on the importance of a sound knowledge of anatomy for the student, and on dissection rather than books for this knowledge. It was some years later that William Hunter, to whom the credit for this innovation is generally incorrectly given, followed where Cheselden had led. He also incorporated in his lectures all that was known of physiology, and was thus the first to conceive the great importance of the preclinical sciences to the medical student. He wrote a famous textbook of anatomy as a companion to his lectures, and this work achieved such popularity that it maintained its place for more than a century. Later he published his great work on the bones of the body, *Osteographia*, and, being no mean artist, he personally assisted in the drawing and the engraving of the illustrations.

In addition to his pre-eminence as a general surgeon—and his speed and success in cutting for the stone had no equal in pre-anaesthetic days—he was a pioneer in ophthalmology. In this connexion his friend Pope wrote:

> I'll do what Mead and Cheselden advise
> To keep these limbs and to preserve these eyes.

At the height of his fame he retired suddenly from the staff of St. Thomas's (just before Percivall Pott was appointed to the staff of Bart's), and took the post of resident surgeon to the Royal Hospital, Chelsea, in order to obtain the necessary time to devote to his great project of separating the Barber-Surgeons Company, of which he was a warden, into its constituent halves. This he achieved by Act of Parliament in 1745, thus freeing surgery for future progress. He was elected to be second Master of the new Corporation of Surgeons.

In addition to his professional attainments Cheselden understood something of architecture and was largely responsible for the plans of the new Surgeons' Hall which was to house his Corporation, as well as those of the new Fulham Bridge, of which he had been elected a commissioner.

In his lifetime he was much liked for his good nature and generosity, and although his professional success aroused jealousy and criticism he refused to be drawn into controversy. Socially he was, unlike most surgeons at that time, born armigerous, and throughout his life in London he was the friend and companion of the "master-spirits" of the age of intellect—such men as Pope, Richardson, and Arbuthnot. He was appointed surgeon to Queen Caroline a few months after her accession, and on several occasions refused the honour of a baronetcy. He became a Fellow of the Royal Society in 1712, and with Dr. Mead attended its veteran president, Sir Isaac Newton, in his last illness.

He died while on a visit to Bath. The *Gentleman's Magazine* described his end as follows: "Mr. Cheselden Esq. an eminent anatomist, lithotomist and surgeon to the Royal Hospital, Chelsea . . . had drank ale after eating hot buns, upon which being very uneasy he sent for a physician who advised vomiting immediately, which advice, had he taken it, it is tho't, might have saved his life." A sad ending to such a distinguished life.

This book, which is well illustrated, should be read by all surgeons, St. Thomas's men, and others who respect the traditions upon which the art and science of medicine (and surgery) are built.

W. S. C. COPEMAN.

MEDICINE IN GENERAL PRACTICE

Modern Treatment: A Guide for General Practice. By 53 Authors. Edited by Austin Smith, M.D., and Paul L. Wermer, M.D. (Pp. 1,146. 147s.) London: Cassell and Company. 1953.

This impressive volume to which 53 American postgraduate teachers contribute is edited by the editor of the *Journal of the American Medical Association* and the secretary of the Association's Committee on Research. It is much more than a textbook of treatment, since considerable space is devoted in each section to physiology, aetiology, pathology, and symptomatology in order that the subsequent discussion of treatment should be rational and not empirical. The work is really a textbook of medicine with emphasis on treatment. In addition chapters are devoted to the principles of pharmacology, immunology, radiology, laboratory procedures, inhalation therapy, and physical medicine, and to the simple surgical, dermatological, and ophthalmological therapeutic principles with which the general practitioner should be conversant.

It is emphasized throughout that the patient should be treated as a whole man and not as a diseased heart, stomach, or lung, and that therapeutics is much more than the prescription of symptomatic or specific medicines. Indeed, the number of drugs mentioned is remarkably small in a book of this size on treatment. In each discussion attention is focused on what, in the author's judgment, is the most effective treatment, but alternative forms of therapy are also critically considered. That there should, here and there, be recommendations with which the reviewer disagrees is only to be expected, but the standard is everywhere worthy of the distinguished authors. All the sections are up to date, well and interestingly written, scientific and yet full of sound practical common sense. The book is beautifully produced and printed. The trouble is that therapeutics is expanding so rapidly that in a few years the work will in parts be out of date, and under the circumstances seven guineas is a lot of money to pay for it.

D. M. DUNLOP.

TOXIC PESTICIDES

Toxic Hazards of Certain Pesticides to Man: Together with a Select Bibliography on the Toxicology of Pesticides in Man and Mammals. By J. M. Barnes. World Health Organization Monograph Series No. 16. (Pp. 129. 7s. 6d.) Geneva: World Health Organization. 1953.

Although pesticides and fungicides have been in use since 1880, the rapid spread of their application on a vast scale has made necessary the fullest possible knowledge of their potential capacity to injure the health of mankind if their object is to be achieved. This object is twofold—the suppression of insect-borne diseases of man, and the reduction of damage to crops sufficiently to ensure adequate nutrition of the world population.

Dr. J. M. Barnes gives us here a timely and valuable contribution to the subject. The book is intended not only for the users of these substances, but also for medical officers and others responsible for public health.

Some countries have attempted legislative control of the new organic pesticides, but a high degree of legal control is difficult, and reliance must be placed largely on the education and training of those who manufacture and apply these poisons. Dr. Barnes frankly admits that there are still many uncertainties about the exact mode and site of

action and even of the precise chemical structure of some of the pesticides, particularly those belonging to the chlorinated hydrocarbon group, of which D.D.T. is a representative. The action of the organo-phosphorus group, including "parathion," is better understood; they act by inhibiting the enzymes which hydrolyse acetylcholine, while the dinitro-derivatives raise the metabolic rate by disturbing vital enzymes and accelerating oxidative mechanisms.

The description of these and other pesticides, as complete as possible in view of the existing gaps in present knowledge, is accompanied by suggestions for control of potential hazards and recommendations for further research, and is completed by an extensive bibliography drawn chiefly from sources in the library of the World Health Organization.

ETHEL BROWNING.

PSYCHOLOGY OF PHYSICAL ILLNESS

Psychology of Physical Illness: Psychiatry Applied to Medicine, Surgery and the Specialties. Edited by Leopold Bellak, M.D. (Pp. 243. £1 17s. 6d.) New York: Grune and Stratton. London: J. and A. Churchill. 1952.

Apart from the introduction by the editor, this book contains articles on the psychological aspects of general practice, internal medicine, malignancy, general surgery, plastic surgery, gynaecology and obstetrics, genito-urinary diseases, orthopaedics, the ear, nose, and throat, neurology, paediatrics, dermatology, dentistry, and the personality of the physician. Of the authors, some well known in their own fields, nine graduated from American schools, the rest from Vienna, Leyden, Prague, Lausanne, Edinburgh, and Groningen. Of the sixteen co-authors nine are psychoanalysts, and most of the remainder have received psychoanalytic training.

These arid details are provided so that the prospective reader may realize how broad are the fields of subject-matter covered, how widely different the backgrounds of the authors, how monotonously uniform their approach. By far the best are the articles written not by psychiatrists and psycho-analysts but by practical workers in the specialty concerned who have merely turned their attention to its psychological aspects. Thus the article by Dr. Haas on psychiatric implications in gynaecology and obstetrics is outstandingly good, and will certainly interest the general medical reader. In much of the rest of the book there is a deficiency of practical clinical knowledge, an excess of theoretical commonplace. Particularly disappointing is the discussion on the psychiatric aspects of neurologic diseases, which is mainly confined to the emotional meaning of illness to the patient. One might have hoped for some discussion of the varieties of psychological experience associated with lesions of particular parts of the brain—for example, the temporal lobe—or with particular types of disturbance of brain function.

ELIOT SLATER.

BIOCHEMICAL TESTS

Scope and Interpretation of the Commoner Biochemical Tests. (Pp. 120. 10s. 6d.) Johannesburg: South African Institute for Medical Research. 1953.

This book gives a judicious account of most of the common biochemical tests, and the author makes no exaggerated claims. Two general criticisms can be made. In the first place, it is now felt that it is not enough merely to give the extreme range of values found in apparently normal subjects. Either some indication should be given of the probability of values that differ from the mean by various amounts, or, at least, the range found in 80 or 90% of normal subjects should be given. It may be possible that total plasma protein as low as 5.6 g. per 100 ml. (the lower level of normal given in this book) may be found in an occasional healthy individual, but such a value should certainly suggest that something was wrong. The second general criticism is that often the author gives no indication of the levels that may be expected in disease.

Certain mistakes and omissions may be noted. Reduction of serum calcium, other than the moderate reduction due to low serum proteins, is not commoner in nephrosis than in nephritis (p. 3). Cholesterol is said (p. 6) to be 30 mg. lower in plasma than in serum; surely this should be lower in whole blood than in plasma. "Secondary prostatic carcinoma" (pp. 10, 92) should presumably be "prostatic carcinoma with secondaries." Estimations of uric acid in serum are more satisfactory than estimations in whole blood. The reader is given little help in choosing between many liver-function tests. Too little is said about tests of water and salt balance.

J. R. MARRACK.

COMPRESSION ARTHRODESIS

Compression Arthrodesis: Including Central Dislocation as a Principle in Hip Surgery. By John Charnley, F.R.C.S. With a chapter on Mechanics by Professor J. A. L. Matheson, and Histological Observations by Professor S. L. Baker. (Pp. 264; 208 figures. £2 2s.) Edinburgh and London: E. and S. Livingstone. 1953.

Mr. Charnley recently stimulated us with an excellent book on the manipulative treatment of fractures. This new volume is a tribute both to his industry and to his versatility.

Compression arthrodesis of the knee has become the accepted technique in Britain because of its simplicity, its certainty, and the speed of union. The author discusses its application to the other joints commonly arthrodesed, but no other joint lends itself quite so easily to this technique as the knee. Charnley has investigated the result of compression in great detail, and its value in accelerating union of cancellous bone seems undeniable. One is still left in some doubt whether compression has a specific effect in stimulating osteogenesis, or whether the complete absence of a gap between the surfaces allows rapid bone union. Whatever the explanation, there is no doubt that this happens at an astonishing speed. This is a delightful book to read and is coloured by the author's vital and forthright comments.

J. I. P. JAMES.

DATA ON RADIOTHERAPY

Roentgen, Radium and Radioisotope Therapy. By A. G. Delario, M.D. (Pp. 371; 65 illustrations. 55s.) London: Henry Kimpton. 1953.

This book is remarkable as a collection by one man of facts, figures, graphs, and tables published before 1951 relevant to radiotherapy. As a radiotherapist I can appreciate to the full the value of the store of easily accessible and thoroughly practical information which the book contains, since in it the necessary data are available for deciding on physical factors required in the treatment of almost any case of malignant or non-malignant condition by *x* rays, radium, or radioactive isotopes. While everyone would not agree with all his suggested doses, all would not necessarily disagree. For instance, I should consider 600 r in six doses of 100 r inadequate for ankylosing spondylitis. The danger of this work is that it might lead the inexperienced to proceed with more certainty than is justified if used in clinical work. Knowledge of technical details is no more a substitute for clinical knowledge and experience in radiotherapy than it is in surgery, and any tendency to ignore this axiom must be deplored. Dr. Delario would, I am sure, be the first to agree with this, since the parts of the book not filled with other people's data contain passages giving glimpses of his comprehensive grasp of the subject.

The book makes me anxious to meet its author, to find out what manner of man he is who displays such industrious ability, eclipsing even that of his *Handbook* of 1938. It is more difficult for me to assess its value to biologists than to medical practitioners, but I feel that no one interested in radiotherapy, the action of radiations, or in the use of radio isotopes would be wasting his money if he bought the book as a work of reference in which to find important technical details at a moment's notice.

FRANK ELLIS.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY NOVEMBER 14 1953

SURGICAL TREATMENT OF MITRAL STENOSIS

A large number of mitral valvotomies have now been performed at many centres both here and abroad, and the operation is firmly established as a successful, and relatively safe, method of treatment. After a few pioneer operations about thirty years ago, including a notable success reported in this *Journal* by Souttar,[1] little progress was made until 1950, when Baker, Brock, and Campbell[2] published an account of six successful operations, the first series in this country. A little earlier Bailey, Glover, and O'Neill,[3] of Philadelphia, had reported eleven successes. By May, 1952, Baker, Brock, Campbell, and Wood[4] were able to describe a series of 100 operations: 13 of the patients had died, but 7 of these were in the first 20 to be operated on. Of 50 patients followed for at least eight months, 32 had a good or an excellent result. In the opening pages of this issue Mr. T. Holmes Sellors and Drs. D. Evan Bedford and W. Somerville describe the clinical and surgical features of 150 cases of mitral stenosis treated by operation, with only four operative deaths. Four other patients died subsequently. Of 110 patients followed for more than three months, 81 have had a good result and 9 others have had worth-while relief of disability.

At present all that the surgeon does at operation is to enlarge the narrowed mitral orifice. If he can do this so as to re-create mobile valve flaps, allowing an increased flow without reflux, a good result will follow. The stenosis is largely due to organization of repeated fibrin deposits, especially between the cusps, where commissures are formed.[5] The operation consists in division of these commissures, and this can usually be accomplished by digital pressure. The type of valve ideal for surgery is the diaphragmatic, for reasons clearly shown by Holmes Sellors and his colleagues. More severe stenosis is accompanied by greater thickening of the valve leaflets and by shortening of the chordae tendineae: valvotomy is the more difficult, a knife must often be used, and normal function cannot be restored. The rigid fibrous funnel of the grossly damaged valve is not suitable for operation, nor, at the present state of knowledge, is the irregular gaping orifice of the incompetent valve.

In selecting patients for operation the surgeon has also to consider the state of the other valves, of the pulmonary vessels, and of the myocardium, though the importance of myocardial damage has perhaps been exaggerated in the past. A patient suitable for surgery must be suffering from symptoms disabling enough to warrant the risk, and these must be due predominantly to mitral obstruction. Breathlessness on exertion is usually the first symptom. Haemoptysis is common, and it is sometimes sudden and massive (pulmonary apoplexy). More serious symptoms are orthopnoea and paroxysmal pulmonary oedema. Attacks of pulmonary oedema usually occur in patients with regular rhythm and a small heart and are a strong indication for operative treatment.

The physical signs associated with a diaphragmatic valve are a tapping apex beat with a snapping first sound and an opening snap—a sharp click following the second sound. Typically there is a loud rumbling diastolic and presystolic murmur, but this may be faint or even absent. The pulse is small. The heart may be enlarged, and in general the larger the heart the more serious the outlook. With mitral stenosis the right ventricle enlarges, displacing the apex beat to the left. Enlargement of the left ventricle, unless the aortic valve is diseased or there is hypertension, is due to mitral regurgitation and is a contraindication to operation. A great enlargement of the left atrium and systolic expansion seen fluoroscopically, especially in the antero-posterior position, also imply severe regurgitation; a systolic murmur is less important. Many stenosed mitral valves which are suitable for operation allow some regurgitation, which should not then prevent operation. Calcification of the valve suggests advanced disease, but may be present in some cases suitable for valvotomy: though an unfavourable feature, it is not a contraindication.

Attacks of congestive heart failure may indicate myocardial damage or a lesion outside the mitral valve; but if the signs suggest a pliant stenosis and if the failure is not of long duration and can be controlled by medical treatment operation should not be withheld. The presence or absence of auricular fibrillation does not influence the decision for or against surgery, except that it is more common in advanced disease. A history of previous embolism is usually considered an indication for operation, because patients who have had one embolus nearly always have others and usually die from this cause

1 *British Medical Journal*, 1925, **2**, 603.
2 Ibid., 1950, **1**, 1283.
3 *J. thorac. Surg.*, 1950, **19**, 16.
4 *British Medical Journal*, 1952, **1**, 1043.
5 Magarey, F. R., *British Medical Journal*, 1951, **1**, 856.

within a few years. An additional risk will be run, since thrombus in the left atrium may be disturbed by the surgeon's manipulations and an operative embolus result. This, however, is not an inevitable complication in such cases. Associated disease of other valves is not a contraindication to operative treatment provided that the disability is principally due to mitral obstruction. Disabling symptoms arising during pregnancy need no longer be considered an indication for termination, since several successful valvotomies have been performed on pregnant women with subsequent normal delivery at term.

When operative treatment has been decided on the patient should be made as fit as possible; preliminary in-patient treatment with digitalis and diuretics may be needed. The method of anaesthesia in these cases requires no special comment, but an intravenous drip of saline with procaine is usually given in the hopes of reducing the likelihood of ventricular fibrillation during operation. A blood transfusion must be ready, but there is usually surprisingly little loss of blood. Most surgeons prefer a lateral or postero-lateral approach through the fifth intercostal space or rib bed. The pericardium is opened and the valve approached by inserting a finger through the left auricular appendage after amputating its tip beyond a clamp. The appendage fits the finger snugly so there is no haemorrhage. Many unsuccessful attempts have been made to devise a method of operation which allows a satisfactory view of the valve, but much can be learnt by palpation. As a rule the commissures can be split by digital pressure: the different patterns of knife available for use when pressure fails suggests that the perfect mitral valvotome has not yet been invented.

The most distressing operative complication is embolism, with an incidence of about 5%. It may occur when no thrombus has been palpated or suspected, and may be due to calcified fragments as well as to clot. The most common site is the brain, and death or permanent hemiplegia may result. Some surgeons believe that compression of the carotid arteries does something to reduce the incidence of this complication. Embolus may also occur in the aorta, and occasionally an aortic embolectomy has been carried out a few hours after a valvotomy. But these complications are the exception, and in most patients recovery is straightforward and improvement immediate and lasting. As yet there is no evidence that recurrence due to re-formation of the commissures takes place. Many patients, completely disabled by distressing dyspnoea, have returned to a normal life and to work. The results obtained by Brock, Holmes Sellors, and other thoracic surgeons are so promising that operation should be considered for every patient who is severely disabled by mitral disease. The decision whether or not to operate can be made accurately on clinical grounds assisted by routine investigations alone. Provided that mitral obstruction is responsible for the symptoms, a good result can be expected.

H. INFLUENZAE AND ANTIBIOTICS

H. influenzae is perhaps more uniformly susceptible to all the major antibiotics than any other species of micro-organism. In the treatment of the most serious infection caused by it—meningitis in infants—we have witnessed the successive trial of penicillin, streptomycin (with or without sulphadiazine and immune serum), and the newer antibiotics—of which chloramphenicol is the most effective, not only because of its high degree of antibacterial activity but because it reaches the cerebrospinal fluid in higher concentrations than any other of these drugs. Nevertheless there are some minor discrepancies in reports of the sensitivity of this organism to different antibiotics, and some findings were based on the study of only a few strains. A comprehensive study of this kind, embracing 34 serologically identified capsulated strains and 50 non-capsulated, is reported by Dr. K. Zinnemann on page 1069. The "punch" or "cup" plate method was used for these tests, and this is apt to give results somewhat unflattering to the drug tested, since its concentration anywhere in the medium surrounding the cup is inevitably less than that of the solution introduced, and diminishes steeply with distance from the margin. More clear-cut results, with lower minimum inhibitory concentrations, are obtainable by mixing the antibiotic uniformly with the medium: by such a method Finland and Wilcox[1] found all their strains of *H. influenzae* to be inhibited by 0.6–1.0 μg. per ml. of chloramphenicol, whereas some of Zinnemann's required concentrations five times greater. A similar difference is observed with aureomycin, most of Finland and Wilcox's strains being inhibited by from 0.6–2 and all by 4 μg. per ml., while some of Zinnemann's were not inhibited by any concentration tested. Whatever the method used, as Zinnemann points out, the relative activity of different drugs can be satisfactorily assessed, and the order of merit based on these tests is chloramphenicol (most active), terramycin, streptomycin, aureomycin. Penicillin ranks with the most active so far as its perform-

[1] *Amer. J. clin. Path.*, 1950, **20**, 735.
[2] *J. Amer. med. Ass.*, 1952, **149**, 231.
[3] Lewis, C. N., *et al.*, *Antibiot. and Chemother.*, 1952, **2**, 601.
[4] *Acta med. scand.*, 1952, **143**, 32.

ance *in vitro* is concerned, but is regarded as therapeutically less useful because the corresponding concentrations are not obtained *in vivo*, at least by any ordinary dosage.

These results may be compared with those given by Dr. A. White Franklin and Professor L. P. Garrod (p. 1067) for strains of *H. influenzae* all derived from the sputum of children with bronchiectasis. Their results were obtained by incorporating the antibiotic in the medium, and there is no significant difference in activity between chloramphenicol, aureomycin, and terramycin, a concentration of 1 μg. per ml. of each of these three antibiotics sufficing to inhibit the growth of all strains (it should be remembered in this connexion that in Zinnemann's tests non-capsulated strains from sources such as this were on the whole more sensitive than capsulated). The variation in sensitivity to penicillin and streptomycin is wider, but the majority were inhibited by 1 and 4 μg. per ml. respectively of these antibiotics. The paper reporting these findings is an account of the results of treating bronchiectasis in children with chloramphenicol. The effect of giving adequate doses was always to suppress the infection, even in severe cases: the sputum became scanty and *H. influenzae* disappeared from it. In some mild cases benefit persisted after treatment was stopped, but in most it continued only during administration of the drug, although a diminished dose sufficed. Treatment for one day in each week was found to be inadequate. This study was brought to an abrupt termination by the death of one of the patients from aplastic anaemia, and it is mentioned that an adult in the same hospital treated with chloramphenicol for *H. influenzae* bronchitis developed the same complication, although he survived it. It may be remembered in this connexion that 2 out of 62 patients treated by Wilson and his colleagues[2] for bronchiectasis with 1 g. of chloramphenicol twice weekly for 5½ and 7 months developed aplastic anaemia, fatal in one of them. He would be a bold man who chose to conclude that the authors of each of these papers had merely been very unfortunate in having seen two cases each of this complication in a comparatively small series of patients. It would be safer to conclude either that the risk is greater from prolonged treatment, although an American survey[3] is said to have elicited no evidence of this, or that some extra risk is involved in the treatment of this particular disease.

If it be agreed that the use of chloramphenicol in the treatment of chronic bronchial infection is unjustified, a powerful therapeutic weapon is lost to us. The high concentrations of this drug in the bronchial secretion, as demonstrated by Franklin and Garrod, may well account for its apparent superiority to other antibiotics. Similar trials of aureomycin and terramycin should evidently be carried out. According to Mulder and his colleagues,[4] who describe an extensive study of chronic *H. influenzae* bronchitis (it is not clear whether some of their 125 adult patients also had bronchiectasis), these two drugs suppressed the infection at least temporarily in most of the small number of patients so treated. The authors obtained their best results by giving both penicillin and streptomycin in daily doses of 4 million units and 2 g. respectively: this treatment eliminated the infection in 50 out of 66 patients, but is presumably feasible only in in-patients.

It has often been truthfully said that the great advances in chemotherapy have done much less so far for sufferers from chronic infections than for those whose lives are in immediate danger. There is scope for further study in this difficult field, and it should not too hastily be concluded that any benefit achieved can only be temporary, especially in the young.

MODIFIED LEUCOTOMY

Operations on the brain, intended by means of a circumscribed lesion to influence some of the symptoms of illness, have now been developed in considerable number. Surgeons have developed techniques of undercutting the cortex or severing the central white matter in different regions of the frontal lobes, of operating directly on the thalamus and aspirating the cingulate gyrus. All these are very different from the so-called standard leucotomy operation which was the prevailing practice ten, and even five, years ago. In a recent issue of the *Journal*[1] Dr. William Sargant described from a wide and varied experience the indications for a modified leucotomy operation. The particular modification of leucotomy to which he directed attention is that in which an attempt is made to confine the injury to the medial inferior quadrant of the frontal lobe, anterior to the tip of the lateral ventricle, so as to divide only this portion of the thalamo-frontal radiation. Those who have had experience of this operation, which has been developed particularly by Mr. Harvey Jackson and Mr. Wylie McKissock, are satisfied that the amount of undesirable personality change produced by it is very much less than that caused by the old standard operation, while its beneficial effects are probably at least as good.

Prefrontal leucotomy is essentially a symptomatic method of treatment, and does nothing for the cure of any disease which may underlie the symptoms for whose relief it is given. Therefore it can be and has been applied in a great variety of conditions. The patients most often selected for operation are schizophrenics; but the reason for this is not that these

1 *British Medical Journal*, 1953, **2**, 800.
2 Kolb, L. C., *J. Amer. med. Ass.*, 1953, **152**, 1085.

patients are especially suitable—often they are not—but that their state is often so severe, so chronic and otherwise intractable, that any measure, even a damaging operation on the intact brain, seems justifiable if it can promise fair chances of some relief. The symptoms which can be relieved by leucotomy are preeminently those of mental distress—states of tension, anxiety, depression, hypochondriacal preoccupation. The operation is therefore of value in relieving intractable pain, as from carcinoma; the relief most commonly seen is that the patient continues to experience pain but is no longer so distressed by it and can apply himself to occupations and distractions. A small proportion of patients who suffer from tinnitus find the noises in the ears unendurable, and are prevented from sleeping, relaxing, or taking the slightest pleasure in any usual interest. They, too, usually benefit from leucotomy, if the gravity of their state is held to warrant it.

However, as Sargant has pointed out, the bulk of the patients for whom leucotomy comes to be considered are those who suffer from psychiatric disorders. In the past these have properly been exclusively patients suffering from psychoses. With the advent of a modified operation which, so far as present experience goes, seems to leave the personality so largely intact, permits a normal social life, and has very little if any ill effect on religious life and ethical attitudes, the time has come when it is right to consider also those patients whose condition is essentially neurotic in nature. Certainly all other reasonable methods of treatment must have received an adequate trial, and the condition must be not only intractable but having a very damaging effect on the life and happiness of the patient. If this is the case, then chronic anxiety states, chronic hypochondriases with marked symptoms of depression or tension, and chronic depressive reactions may all arise for surgical consideration. It is in only a small proportion of cases of these kinds that the indications will be thought to be adequate; but surgery does hold out hope to some of the worst cases at a price which now seems more reasonable than of old.

As has recently been brought out by Kolb[2] in a review of the results in about 10,000 cases in the United States, one of the prerequisites for successful surgical treatment of severe psychiatric illnesses is the possibility of adequate aftercare. The attitude of the relatives is of supreme importance. If they are prepared to give the patient a new chance, to make allowance for his remaining deficiencies, and to take some personal responsibility in his rehabilitation, then the chances of a good result are much improved. Operative treatment is only one part, even if it is the most significant one, in the whole plan of treatment in those cases in which it is applied. The doctor must be prepared to maintain his interest in his patients after operation, to continue to help them on their way, as Sargant has emphasized, by all the psychotherapeutic and somatic methods they may require, even after the six to twelve months it takes for operation to show its full effects. The principle of therapeutic persistence is one which, here as elsewhere, brings untold benefit.

PLANTAR WARTS

The literature on the infective wart is peculiarly barren. There are few people on whom the impudent visitor fails to call at some time in life, yet our knowledge of the natural history of the disease, our understanding of its aetiology, and the approach to treatment leave much to be desired. It might be thought that a lesion so common and so accessible, associated as it appears to be with the presence of a virus, and producing a wide variety of intriguing pathological patterns of a neoplastic character might provide an important field of research for the experimental pathologist and the virologist. Yet little is written that could not be contributed by the lay wart charmer. It is doubtful if the legitimate practitioner, even when he enlists the services of his psychiatric colleague, approaches the therapeutic success of this unqualified competitor.

The age incidence of warts, the great modification of them produced by the different textures and other characters of the skin affected, and the variable course of the disease in different individuals, variations which may run parallel with changes in the physical and emotional health of the patient, point to the importance of the soil as well as the seed in this disease. Perhaps the discovery of an effective viricide would simplify treatment and make considerations of soil irrelevant, but that day is not in sight. At present the assessment of most methods of treatment is vitiated by ignorance of the psychological factor, which can so modify the skin as to render it unreceptive to the infective wart.

Plantar warts behave in the same manner as warts at other sites, but call for general consideration. The thickness of horn and the trauma of walking drive the warty growth in towards the dermis instead of allowing it to develop outwards. This outward growth in fact occurs if the patient avoids walking and is rested in bed. The pressure on the dermal papillae, by causing pain, may lead to orthopaedic faults, and for this reason plantar warts demand treatment.

Whitfield[1] recognized two patterns of plantar wart. The first was dependent on trauma resulting from deformity of the foot or from an irregularity in the sole of the boot, and its cure rested upon correction of this fault. The other type of the simple infective variety was often multiple and particularly affected the site of tread. That moisture favours the growth and exuberance of warts seems evident, and many forms of treatment clearly benefit by their desiccating effect. Branson and Rhea,[2] from their experience of treating forty-eight soldiers with plantar warts in the American Army, claim success from the injection of 1% procaine into the stratum germinativum exactly under the wart. That last injunction perhaps only emphasizes that once again we are reading the results of treatment by suggestion. The procedure must be a very painful one.

There are two lines of treatment for infective warts, no matter what their site. Plantar warts must undergo radical removal or destruction. This is most satisfac-

1 *Brit J Derm.*, 1932, **44**, 580.
2 *New Engl J Med.*, 1953, **248**, 631.
3 Morgan, J. K., *Brit. J. Derm.*, 1952, **64**, 55.
4 Ibid., 1943, **55**, 267.

torily achieved by curettage under anaesthetic or after freezing by carbon-dioxide snow or liquid nitrogen,[3] less satisfactorily by diathermy or a destructive dose of *x* rays. There has quite rightly been much outcry against the use of *x* rays, and undoubtedly it is improper to produce radiotherapeutic damage of the foot in the treatment of so benign a lesion as a wart. Even so, if properly conducted, the treatment may be both successful and safe.

Other forms of treatment depend essentially on suggestion, though some combine with it some degree of destruction or desiccation. Perhaps the most useful is Thomson's treatment with 3% formalin.[4] The wart or warts are placed in contact with the solution in an egg-cup for ten minutes each day for six weeks. Less certain measures are adhesive strapping with or without 25% podophyllin in oil and fractional doses of *x* rays. Astringent foot baths and powders are of some prophylactic value, especially where there is hyperidrosis.

SUNLIGHT AND MILK

Milk is often exposed to sunlight for long periods. It may be exposed in the van during delivery and later on the doorstep, particularly at week-ends, when the milk bottle left at the side door is a common sight. This exposure to light affects not only the vitamin content of the milk but also its flavour. Considerable quantities of the riboflavin of milk are inactivated by exposure to ultra-violet light, and as much as 50% of the ascorbic acid may be destroyed if milk is left in bottles exposed to bright sunlight for an hour or so.[1] The change in flavour of milk exposed to light seems to be associated with the presence of sulphur-containing compounds.

According to Patton and Josephson[2] the objectionable flavour is due to the presence of a compound produced by the photochemical decomposition of the sulphur amino-acid methionine, the reaction being accelerated by riboflavin. These workers suspected the importance of methionine in this connexion when they observed that dilute solutions of methionine itself exposed to sunlight developed a flavour identical with that produced in milk treated in the same way. Further examination of the problem showed that the addition of methionine in amounts as small as 4 mg. per quart (1.1 l.) intensified the flavour in skim-milk exposed tc sunlight. The process is undoubtedly photochemical, for it depends on the time of exposure and the wavelength of the light, and is independent of temperature. The readiness with which the flavour developed in skim-milk in comparison with solutions of methionine alone suggested that one of the constituents of milk activated the process. It was suspected that this might be riboflavin, which absorbs light and is a component of an oxidation-reduction enzyme system. Patton and Josephson observed that exposure of a solution containing methionine and riboflavin to light developed the flavour to a much greater degree than one containing methionine alone; riboflavin solution alone developed no flavour. Other sulphur-containing amino-acids, such as cysteine and cystine, were tested, but were not found to be associated with the production of the "light" flavour, which seems to result specifically from the photolysis of methionine in the presence of riboflavine.

Whatever the mechanism of the process, milk should be exposed to sunlight as little as possible if its flavour and vitamins are to be preserved. The use of milk bottles made of dark glass would minimize the effect of light on the milk, and as the breakage rate of bottles is very high the gradual replacement of existing stocks would not take very long.

[1] Holmes, A. D., and Jones, C. P., *J. Nutr.*, 1945, **29**, 201.
[2] Patton, S., and Josephson, D. V., *Science*, 1953, **118**, 211.

ELECTRONIC EYES?

Someone recently asked St. Dunstan's whether television could somehow be adapted to help the blind to see. This is a recurring theme with each new invention. When the full story of science's part in the war was published radar was proposed as a substitute for sight, and an article in this *Journal*[1] explained why centimetric radio waves were unsuitable for any form of blind aid, and described some research done at St. Dunstan's and elsewhere on ultrasonic aids which were more promising. It was then pointed out that all instrumental aids faced some general difficulties. They had to be very small and light or no one would wear them for long. They had to be simple to control and maintain. All of them took time to learn to handle, and it was found that where a blind person was prepared to spend the necessary effort on a course of instruction—and, since the majority of the blind are elderly, this is not always the case—the end-results were less good than if the same effort had been expended in developing the other senses. In other words the blind man does better by improving his use of his own body than by calling in any of the tools science can offer.

But can science offer electronic eyes? Dr. E. D. Adrian[2] has explained in a recent issue of the *St. Dunstan's Review* why this is at present impossible. Sensation of light or movement of a crude kind can be produced by stimulating the surface of the cerebrum directly, but to leave electrodes in contact with the brain surface for more than a short time is risky, while contacts on the scalp outside the skull are obviously too distant for precise localized stimulation. Furthermore, "the visual messages from the eyes do not go straight to the cerebral cortex and to nowhere else; they go through an elaborate nervous apparatus in the retina and in the brain stem, so that what arrives in the cerebral cortex is not just a reproduction of the pattern of light and shade falling on the retina." We do not at present know enough about the retinal events and their relation to the conscious events which constitute vision, but even if we did the pattern of electrical microstimulation required might well prove impossible to produce. Research in other directions will be more profitable.

[1] Beurle, R. L., *British Medical Journal*, 1951, **1**, 1319.
[2] *St. Dunstan's Review*, 1953, **38**, 8.

CLINICAL PATHOLOGY IN GENERAL PRACTICE

TAKING SWABS

BY

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Use of the cotton-wool swab mounted on a wire or wooden applicator for the collection of material for bacteriological examination from various body surfaces and cavities is some 60 years old. Recommended by Councilman in 1893, it was first used in Britain by Hewlett and Nolan (1896) and by Preston (1896) for the isolation of diphtheria bacilli from the throat of affected patients. It has since been widely utilized for the collection of secretions or discharges from the nose, nasopharynx, larynx, trachea, eye, ear, skin, superficial and deep wounds, rectum, vagina, and cervix. The purpose of this article is to discuss the kind of swabs to be used and the best method of collecting material from the sites mentioned.

The Swab

The swab commonly consists of a small pledget of cotton-wool wrapped tightly and smoothly round the roughened end of a wire or wooden applicator in such a way that no part of the end of the applicator is left exposed and there is little risk of the swab being pulled off during the collection of the specimen. This latter requirement is particularly important for nasal, cervical, and rectal swabs. The swab should not be bulky, and for pernasal use should be small enough to avoid unnecessary irritation to the nasal mucosa when being passed back to the nasopharynx. Although the use of absorbent cotton-wool is usually recommended, it is probably more advantageous for the survival of bacteria on plain swabs to use non-absorbent wool (Rubbo and Benjamin, 1951). As regards the applicator, wire is more flexible than wood, but the metal should not be too pliable, as aluminium tends to be: "nichrome" wire is now widely used, but stainless-steel wire, which can be hooked at the end to retain the swab, is also favoured. The wooden applicator is recommended for use with the serum swab (see below) to avoid the discoloration which may result from the interaction of the serum with a metal, although this risk should not occur with stainless-steel wire. The applicator is usually pushed into or through a cork at the holder end, and the whole swab is assembled in a test-tube container.

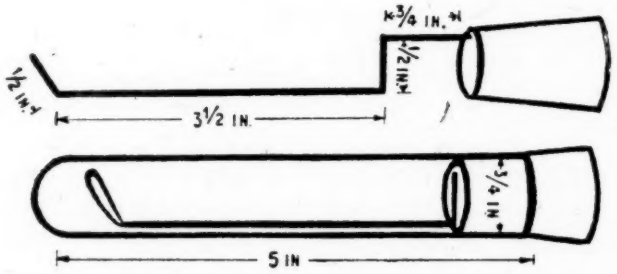

FIG. 1.—Nasopharyngeal swab for use through the mouth.

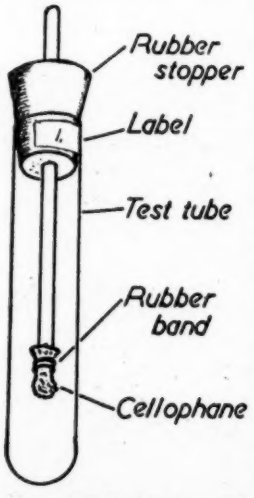

FIG. 2.—Perianal swab for threadworm ova.

Swabs of special design are used for the collection of material from particular sites. West's swab in a bent glass tube for swabbing the nasopharynx is now an anachronism: instead the ordinary throat swab with a flexible wire holder may be bent to an obtuse angle (about 120 degrees) ½ in. (1.3 cm.) from the tip and used with a tongue depressor to avoid mouth contamination. The swab described by Tarr (1946) for post-nasal culture is illustrated in Fig. 1. For pernasal swabs fine nichrome (S.W.G. 25) or stainless-steel wire with a hooked end is recommended (Cockburn and Holt, 1948). In collecting material from the conjunctiva some ophthalmologists prefer to use the wire loop, which is inoculated directly on to the culture medium, but a fine cotton-wool swab may be used instead. For laryngeal swabs the choice lies between nichrome wire (S.W.G. 16) and stainless steel, which is rather more rigid: the applicator is 9 in. (23 cm.) long and bent at an angle of 120 degrees about 2 in. (5 cm.) from the tip, and is placed in a large test-tube container (8 by 1 in.—20 by 2.5 cm.).

For obtaining faecal material with a swab passed into the rectum and for swabbing the vagina or cervix, the ordinary throat swab with a 6 in. (15 cm.) long applicator is best. A special type of perianal swab is used for collection of roundworm ova. It consists of a 2 cm. square of plain transparent non-moisture-proof "cellophane" wrapped about the tip of a small glass rod and held in place with a rubber band. The holder end of the rod is pushed through a cork stopper and the whole swab placed in a test-tube container (Fig. 2).

The Serum Swab and Bacterial Survival

A major concern in the use of the cotton-wool swab is the period of viability of pathogenic bacteria on the swab between collection of the material and its inoculation on to appropriate culture media. Because of the poor viability of certain bacteria like the gonococcus and the meningococcus material suspected of containing these pathogens is best inoculated on to suitable media as soon as the swab is taken; but this procedure has obvious disadvantages, and various substitute methods for allowing an interval of time between collection and inoculation of these poorly viable bacteria have been recommended. For example, Stuart (1946) found that gonococci could survive for 24 hours or longer if the swab on a wooden applicator is immersed in Brewer's medium before transportation to the laboratory: a somewhat similar procedure was recommended by Saint-Martin (1949), who used Hirschberg's medium as the vehicle. Downie (1940) found that meningococci on nasopharyngeal swabs could be cultured 24 hours after swabbing if the swab were immediately placed in contact with blood agar in the bottom of the container, while Aycock and Mueller (1950) recommended immersion of the swab in horse blood for the same purpose.

The problem of bacterial survival is not confined to the *Neisseria*, since slow-drying is known to be lethal to most bacterial species. The matter has been extensively investigated by Rubbo and Benjamin (1951), who, as a result of their comparative findings with many different pathogens, recommend the use of a serum-coated cotton-wool swab. The swabs are prepared by dipping the cotton-wool swab on a wooden applicator into undiluted ox serum for 10–30

seconds, spreading them out on sheets of blotting paper, drying in an incubator at 37° C. for about half an hour, and finally sterilizing in the autoclave at 15 lb. per sq. in. (1 kg. per cm.^{2}) for 20 minutes. The finished product is a compact honey-coloured pledget, 3–5 mm. in diameter, in which the cotton-wool fibres are firmly bound to each other and to the applicator.

Rubbo and Benjamin found that, with the exception of the *Neisseria*, the serum swabs prolonged survival and gave heavier growths (compared with plain swabs) of some 16 different bacterial pathogens. In addition, they showed that moistened plain swabs but not serum swabs accelerated the death rate of Gram-positive bacteria like *Str. pyogenes* and *C. diphtheriae*, whereas the survival of the Gram-negative intestinal pathogens like the typhoid bacillus and Flexner and Sonne dysentery bacilli was prolonged in the absence of moisture. The deleterious effect of moisture and slow drying on the viability of *Str. pyogenes* and *C. diphtheriae* has a direct application to the moist throat swab, which with plain cotton-wool is unlikely to give reliable results if there is a delay of twenty-four hours between collection and inoculation. For example, in an outbreak of scarlet fever 170 miles from Melbourne the Australian workers found that plain and serum swabs cultured on blood agar twenty-four hours after collection gave respectively 23% and 39% positive isolations of *Str. pyogenes*. Variations in atmospheric temperature (15–24° C.) were unimportant, but *Str. pyogenes* survived rather longer on swabs left in the refrigerator (4° C.) than at room temperature, whereas *Sh. flexneri* did not.

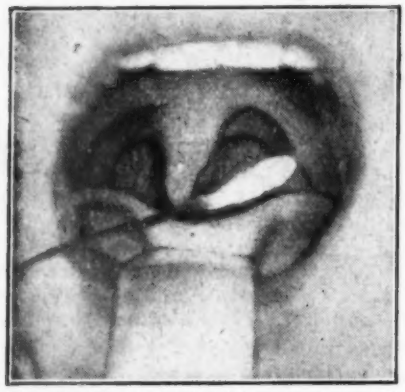

FIG. 3.—Throat swab with a clear view of the fauces.

The quality and origin of the cotton-wool have little effect on survival time, and cotton-wool does not seem to contain any toxic lipoid substance, although there is some evidence that gonococci survive better in discharges collected on linen rather than on cotton-wool (see Mackie and McCartney, 1953). If, then, the serum swab is used, and assuming a moderately heavy coating with the suspected pathogen, bacteriological examination of such material usually yields a valid result when cultured within the following time limits :—(1) organisms viable for less than eight hours : gonococci and meningococci (see alternative methods listed above) ; (2) organisms viable for eight hours : *H. pertussis, C. diphtheriae, V. cholerae* (moist swab); (3) organisms viable for twenty-four hours : haemolytic streptococci, pneumococci, *Str. viridans*, and *Cl. welchii*; shigellae and salmonellae on moistened swabs ; and (4) organisms viable for forty-eight hours ; staphylococci, coliform bacilli, proteus, and pyocyanea.

Throat Swabs

The throat swab is used principally to collect material from the faucial area in patients suffering from acute pharyngitis or tonsillitis or suspected Vincent's angina, and in the detection of contact, convalescent, or chronic carriers of haemolytic streptococci or *C. diphtheriae*. The operator must have a clear view of the whole fauces in a good light and see the swab touching the affected surfaces (Fig. 3). The patient should be sitting up or standing with the head tilted back ; with children or nervous patients an assistant should support the back of the head with one hand, to prevent sudden or unexpected movement, and hold the patient's hands with the other. If good natural lighting cannot be obtained a hand torch must be used ; some tongue depressors have an illuminated tip which does equally well. It is wise to use a tongue depressor even with patients whose throats can be clearly seen. It should be placed in one movement firmly on the back of the tongue, after which the swab is inserted and rubbed over the faucial area, gently if the throat is acutely inflamed, more vigorously if searching for carriers. In suspected chronic tonsillar carriers or infections the swabbing may be preceded by pressure with the fingers on the tonsils to squeeze out secretion in the tonsillar crypts. When Vincent's angina or moniliasis is suspected two swabs should be taken, as one will be required for the preparation of smears for direct microscopical examination, which, however, has little or no value in other acute throat infections. Throat swabs are preferred to throat washings for the isolation of poliomyelitis virus from the oropharynx.

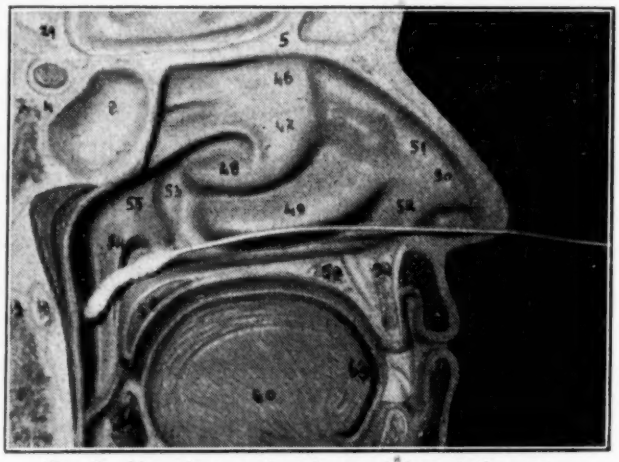

FIG. 4.—Nasopharyngeal swab passed through the nose.

Nasopharyngeal Swabs

Some pathogenic or potentially pathogenic bacteria that colonize the upper respiratory tract are to be found predominantly in the nasopharynx or post-nasal space. These include the meningococcus and pneumococcus, and in whooping cough *H. pertussis* is most conveniently isolated by nasopharyngeal swabbing. This area may be reached with a swab passed through either the mouth or the nose. The peroral swab with its bent tip is passed to the back of the throat—a tongue depressor is essential—and then slipped up behind the uvula to the post-nasal space. In infants it may be very difficult to pass the swab up behind the uvula, and instead the tip may be directed downwards to the posterior pharyngeal wall. The pernasal swab is passed more or less horizontally along the floor of the nasal passage (Fig. 4), with the patient's head held firmly because of the natural

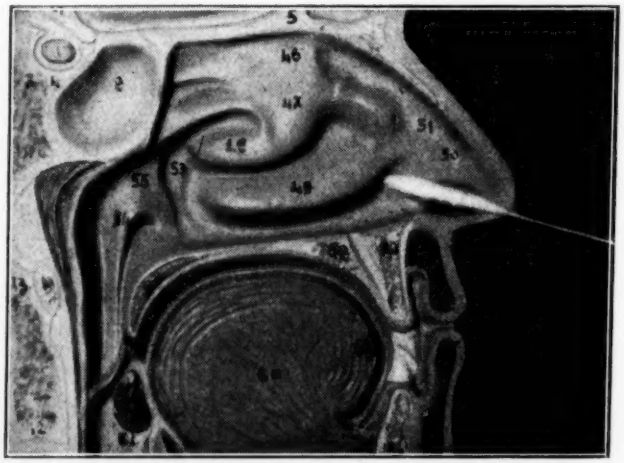

FIG. 5.—Swabbing anterior nares for staphylococcal carriers.

tendency to withdraw. If contamination with bacteria in the anterior nares is to be avoided, a nasal speculum should be used.

Nasal Swabs

Swabs may be taken from two different sites in the nasal cavity as well as from the post-nasal space. A high proportion of the population carry *Staph. aureus* in the nose, and this organism is found particularly in the vestibule or entrance to the nostrils, where it multiplies on the moist invaginated squamous epithelium. In searching for staphylococcal nasal carriers, therefore, it is sufficient to rub a moistened swab round the vestibule of both nostrils (Fig. 5). If, on the other hand, material is to be examined for infection of the nasal mucosa or associated paranasal sinuses, the swab should be rubbed over the turbinates. Similarly in searching for nasal carriers of pathogens like *Str. pyogenes* or *C. diphtheriae* and in obtaining swabs from young children with suspected pneumococcal respiratory infection the swab should be inserted ½–1 in. (1 to 2.5 cm.) into the nasal cavity, again using a speculum if contaminants from the vestibule are to be avoided.

Laryngeal Swabs

The laryngeal swab has only recently come into frequent use for obtaining lung secretions in early suspected cases of pulmonary tuberculosis or in convalescing patients who have become sputum-free. With a little experience, at first using a laryngeal mirror, the doctor will find that for this purpose the laryngeal swab has advantages over stomach washings, in that the patient is more willing to co-operate in having repeat swabs taken. The bacteriologist also prefers it because it is easier to handle. It is, however, essential that the swabs should reach the laboratory within a few hours of being taken.

The patient, sitting up and with his head tilted back, is asked to open his mouth widely. The operator, who should wear a mask, catches the tongue in a gauze swab and pulls it forward so that the patient tends to "gag." The laryngeal swab is dipped in sterile water or saline and then with or without the aid of a mirror is passed down into the larynx, when the patient may be asked to cough but usually does so without being asked. Two successive swabs should be taken, placed in the test-tube container, and transported by messenger to the laboratory as quickly as possible.

Eye Swabs

Swabs may be taken from the conjunctival mucosa when it is inflamed or as a preliminary to operations on the eye to exclude the carriage of pathogenic bacteria. The patient is asked to look up. The lower lid is everted and a fine swab is rubbed gently along the conjunctival surface.

Ear Swabs

Infection of the ear may occur in the external meatus or in the middle ear. In otitis externa a fine swab is rubbed gently over the inflamed area. In suppurative otitis media accumulated discharge must first be cleaned away before the swab is taken, preferably through an aural speculum, so that if possible the bead of pus oozing through the perforated membrane is collected.

Skin Swabs

Swabs may be taken from the intact skin in searching for carriers of pathogenic staphylococci among food-handlers in an outbreak of staphylococcal food-poisoning or among hospital staff and patients in outbreaks of staphylococcal infection—for example, wound infection, pemphigus neonatorum, or lactation mastitis. Moistened swabs should be rubbed over the skin of the fingers, back and front, or an area of about 1 sq. in. (6.5 cm.^{2}) on the back of the wrist may be swabbed.

Rectal Swabs

Swabs may be taken from the rectum for the bacteriological diagnosis of infantile gastro-enteritis, bacillary dysentery, or enteric fever, but in spite of the advantages of the rectal swab in convenience and hygiene of collection it does not allow the full examination for parasites, etc., that is possible with a specimen of faeces. The rectal swab has been used particularly in swabbing groups of young children in day or residential nurseries during outbreaks of Sonne dysentery to find out quickly the incidence of cases and carriers in the group. Whenever it is used, it is important to ensure that, with the patient lying on his side, the swab is pushed well into the rectum and that it is covered with faecal material when withdrawn. The swab must be cultured within a few hours of collection unless some method for keeping it moist is adopted. It is most convenient for collecting specimens from young children; in children over the age of 3 years the doctor should for psychological reasons explain to the patient what he intends to do. It is unnecessary to use a speculum in collecting specimens from children under 5 years of age, but a specially made glass or rubber speculum may be used in older children and adults.

Perianal Swabs

In suspected cases of threadworm infestation a special swab (see p. 1095) may be used to collect scrapings from the anal region, where the ova are frequently found. The edge of the cellophane swab is scraped through the perianal folds and the swab is then transported in the test-tube container to the laboratory, where the cellophane is removed and the swab placed faeces side down in a drop of N/10 sodium hydroxide.

Vaginal or Cervical Swabs

Vaginal discharge may be derived from inflammation of the vagina itself as in trichomonal infection and the vulvo-vaginitis of children, or from the cervix or uterus as in gonococcal and puerperal infections. For the bacteriological examination of most of these infections in adult women the practitioner will find it most practicable to take a high vaginal swab with the patient lying on her side. The external labia and perineum should first be cleansed with warm water, swabbing towards the rectum in one movement. A Cusco bivalve speculum or a Sim duckbill speculum is introduced and an ordinary throat swab is passed into the posterior vaginal fornix. A cervical swab can be taken satisfactorily only with the patient in the lithotomy position, when with a Cusco speculum the cervix is exposed and the swab introduced. In cases of suspected trichomonal infection some of the discharge should be collected with a Pasteur pipette, which is then sealed with plasticine so that the fresh specimen can be examined as a wet film under the microscope. But a swab may be used, provided enough of the discharge can be collected to allow preparation of the wet film.

For the vulvo-vaginitis of childhood the patient should be lying in the dorsal position with the knees drawn up and the thighs separated as far as is possible without hurting the child. Any superficial discharge is removed and the external genitalia are separated with gloved thumb and first finger of the left hand. The swab must be pushed well into the vagina and withdrawn with some discharge on it. The first swab is used to prepare a smear and the second for inoculation on suitable culture media as soon as possible.

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Next article on Clinical Pathology.—"The Collection of Forensic Specimens," by Dr. Donald Teare.

Nova et Vetera

THE STUDY OF MEDICINE AT THE UNIVERSITY OF COPENHAGEN, 1537-1645

Dr. E. Gotfredsen has recently reviewed[1] the medical history of the University of Copenhagen with a happy blend of nostalgic piety and gentle irony. The year 1537 is noteworthy for the re-establishment of the University of Copenhagen by King Christian III after the storms of the Reformation had subsided. Two years later the King undertook to uphold the spirit of the restored university with "good professors" honourably paid. The payment was 140 daler yearly—a rate of pay which Professor Erik Warburg has lately found to be equivalent to that enjoyed by "good professors" at the present time when due allowance is made for the cost of living then and now. A professor of theology received 10 daler more a year, but a professor of law had to be satisfied with only 100 daler yearly, and the stipend of a professor of philosophy was down to 70 daler. But, if numbers count, the faculty of philosophy was better represented with its eight professors than the faculty of medicine with its modest two. Professors of medicine had not only to teach but also to attend the sick at Court and at the university as well as the nobility in the provinces.

The range of subjects which the professors of medicine had to teach the young was quite impressive. Lectures were given on mathematics and astronomy, and enough had to be known of the latter to enable a professor of medicine to edit an almanac every other year. Astrology was also included in the syllabus in so far as it had to be invoked in the drafting of a horoscope, but professors were warned to walk gingerly in this particular field, "as Christians should avoid all superstition." The subjects to be lectured on were strictly defined in advance, and the lectures of physicians and theologians were modelled on much the same lines, with only this difference—that for the physician Hippocrates took the place of Luther and Galen the place of Melanchthon as sources of inspiration.

Professors of medicine began their lectures in Latin at 6 a.m., so they may well be excused for having drifted into rather slovenly ways, just reading from a text faithfully taken down as dictation by students happy to absorb knowledge in so simple a way. But this easy system of conveying knowledge by dictating Latin quotations seems at one time to have incurred royal disfavour, for in 1621 King Christian IV complained that "we have also learnt that many of the professors spend most of their time in dictating what they have culled from various other authors in order to save themselves trouble." The royal rebuke continued: "The university is not specially founded for the maintenance of the professors, but solely to the glory of God and for the promotion of youth. We graciously adjure you to discontinue useless dictation so that you can get through your curriculum in the course of a year."

The lectures on medicine were confined to theory and not supplemented by demonstrations of patients, anatomical preparations, drawings, and the many other devices for relieving the monotony of the spoken word. A student could well become a doctor of medicine without having seen a single patient or learnt how to diagnose a disease. But he had wonderful opportunities to acquire facility in debate when he took part in *disputationes* on set subjects. Four times a year a professor of medicine had to supervise and guide medical students in such debates. In 1617 the subject of debate was: "Is the patient suffering from pleurisy to be bled on the diseased or healthy side at the onset of his illness?" This was a terribly knotty question, for Greek and Arabic authorities disagreed over it. Now, with the omniscience of to-day, it is easy to anticipate the correct answer to this question. Bleeding was to be undertaken on the healthy side at the onset of the pleurisy in order to convey blood away from the diseased side. "To bleed on this side would merely mean a flux of new blood, a hyperaemia which would aggravate the inflammation."

CLAUDE LILLINGSTON.

[1] *Ugeskr. Læg.*, 1953, 115, 540.

A "SMOG" EXHIBITION

This month the Royal Sanitary Institute is staging at its headquarters at 90, Buckingham Palace Road, London, S.W.1, a seasonable exhibition illustrating "smog," its causes and effects, and the way to get rid of it. Large-scale models and diagrams impress the visitor with the results of investigations into atmospheric pollution, the damage it causes to health and property, and the advantages of smokeless fuels. From the experience of London last winter atmospheric pollution is not a diminishing quantity, but it is some satisfaction to know that at any rate its measure is being taken. Special instruments for measuring pollution are now established on 870 sites all over the country, and the amount of grit or deposited matter, of smoke or suspended matter, and of sulphur dioxide is carefully recorded. Local authorities, nationalized industries, and commercial undertakings to the number of 175 are co-operating regularly with the Fuel Research Station of the Department of Scientific and Industrial Research in this enterprise.

The effect of the week of "smog" in London in the early part of last December is driven home pictorially, statistically, and in other ways in this exhibition. The maximum concentration of sulphur dioxide in Westminster and eastwards along the Thames during that week was four or five times the normal, while the number of deaths in London ascribed to bronchitis, pneumonia, and diseases of the heart and circulatory system reached a startling level, more than two and a half times as high as the level of the previous week. Another exhibit shows the effect of atmospheric pollution on livestock. The bones of cattle which had grazed on pasture heavily contaminated with fluorine showed exostoses and other changes. Masonry is liable to attack, and this is well shown by stone from the Houses of Parliament, where the acid-laden smoke has destroyed the beautiful incised decoration. The same is true of metals. The British Iron and Steel Research Association demonstrates the results of tests on copper-steel and zinc at 16 sites in Great Britain, and the difference between the Surrey countryside and places like Sheffield from the point of view of corrosion is well brought out.

Belching Chimneys and Smokeless Zones

The domestic fire is arraigned by the National Smoke Abatement Society as responsible for half the 2,500,000 tons of polluting matter which is sent forth from the chimneys of Great Britain each year. An exhibit of smokeless fuels—anthracite, dry steam coal, gas, and hard cokes—points the way to a remedy, and shows also that hygiene is a paying proposition, for such fuels have a higher standard of heat efficiency. Diagrams also illustrate the creation of smokeless zones in which all pollution is prohibited. These can be of any size from a few acres upwards, including the square mile of the City of London, which it is proposed shall be one of them. Much also can be done in the factory to prevent air pollution, for instance, by the use of efficient dust and fume extractors. Another aid is a new type of fire door, developed at the Fuel Research Station, which is said to eliminate smoke and at the same time to increase thermal efficiency. In the ordinary way a Lancashire boiler will emit as much as 30 lb. of solid matter in an hour, and up to 15% of the heat in the fuel goes to waste.

The exhibition does not include means of individual protection such as have led to recent controversy; the effort is made to indicate causes, and in diagram, poster, and leaflet the solution looks simple. However, if any visitor is inclined to excessive optimism, he may be reminded that the very last patent taken out by James Watt was for the construction of a furnace in such a way as to avoid smoke. That was in 1785. The principle was all right; the difficulty lay in its practical acceptance. That is where the difficulty lies to-day.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Treatment of Tetanus

SIR,—In his article on the treatment of tetanus, Dr. J. H. McIntyre (*Journal*, October 17, p. 866) advocates active immunization of babies against tetanus at the same time as the routine immunization against diphtheria.

Mr. A. T. Glenny and I have investigated the antitoxic responses of young babies to a combined prophylactic containing purified diphtheria and tetanus toxoids and whooping-cough vaccine. We are indebted to Dr. N. R. Butler, of University College Hospital, for the clinical side of the work.

Of a group of 64 babies receiving three injections given at the ages of 6, 12, and 18 weeks, 61 had produced at least 1 unit of tetanus antitoxin per ml. at the age of 6 months, and the remaining three had shown satisfactory responses. All babies born with 0.1 unit per ml. or less of passive maternally conferred diphtheria antitoxin (cord-blood titre) responded actively to the diphtheria toxoid in the prophylactic. In some of those with higher cord-blood titres interference occurred through neutralization by the passive antitoxin, but a delayed response may take place.

Although the majority of babies would be adequately primarily immunized against both diphtheria and tetanus by the course we adopted, I would recommend that the first dose should be delayed until the age of 3–4 months. The dosage of the two toxoids was such as to give good immunity to both components in normal animals. The presence of maternally conferred immunity, however, not only reduces the effectiveness of the diphtheria toxoid but upsets the balance of the prophylactic: as a result additional interference with the diphtheria toxoid may occur because tetanus toxoid is then in excess.[1] By waiting until babies are 3–4 months old before starting immunization, the maternally conferred diphtheria antitoxin would have fallen sufficiently in almost all.

We hope to publish our results fully in the near future.—I am, etc.,

MOLLIE BARR.

The Wellcome Research Laboratories, Beckenham, Kent.

REFERENCE

[1] Barr, M., and Llewellyn-Jones, M. (1953). *Brit. J. exp. Path.*, 34, 12.

SIR,—I read Dr. J. H McIntyre's paper on the treatment of tetanus (*Journal*, October 17, p. 866) with interest, and I would like to make some comments on the very important point he raises.

A study of papers published during the past few years on the treatment of tetanus with relaxants shows a higher proportion of recoveries than is usual in any large consecutive series treated by older methods. This might indicate that these new drugs were lowering the mortality, but allowance must be made for selection and the human tendency to publish successes rather than failures. Tetanus is a disease in which a comparatively accurate prognosis can be given 48 hours after the onset if certain observations are made, and provided that a large dose of antitoxin is given. Prognosis depends particularly on the presence or absence of local tetanus involving either the eyes, face, or limbs; the severity and type of wound; the length of the incubation period; and the length of the period of onset. The incubation period is the time between receipt of the wound and the onset of the first symptom—usually trismus. The period of onset is the time between the onset of the first symptom and the occurrence of the first reflex convulsions.

Prognosis is invariably good when there is local tetanus and usually so if the wound is very slight, if prophylactic antitoxin has been given, and if the incubation period is more than 10 days. It is bad if the wound is severe and heavily infected and the incubation period is less than five days. The period of onset gives the best indication of the severity of an attack. If this is less than 48 hours the prognosis is bad and the patient is unlikely to recover. If it is more than 48 hours there is a good chance of recovery and this increases with every hour the reflex convulsions are deferred. The above observations usually support each other—that is to say, a patient with a severe wound usually also has a short incubation period and a short period of onset and vice versa—but if there is disagreement the period of onset is the most reliable prognostic indication. As Dr. McIntyre states, both his cases were very severe, with incubation periods of four and six days respectively and a very rapid onset of reflex convulsions giving a period of onset of considerably less than 48 hours in both. Neither had any chance of recovery unless relaxants could have worked a miracle.

By contrast and using the same criteria, some of the cases which have been reported would manifestly have recovered on routine treatment whether relaxants had been used or not. In many the essential data by which prognosis could be assessed is omitted, and so the part played by relaxants in furthering recovery is not as clear as it might be. My own limited experience with mephenesin suggests that, although this relaxant is of considerable value in controlling or lessening the severity of spasms, especially in mild cases, it has little effect in very severe ones like those described by Dr. McIntyre. In one patient with a period of onset of about 48 hours in which the prognosis was borderline recovery occurred. Here mephenesin may have tipped the scales towards recovery, and it is probably in cases of this degree of severity that relaxants may save life.

The purpose of this letter is to urge that when reports of tetanus patients treated with relaxants are published all the above data should be included so that they can be used as a yardstick to assess prognosis and to give a more accurate estimate of the value of any drug used. In the present state of knowledge treatment of tetanus is but symptomatic. Death or survival depends almost entirely on the dose of toxin absorbed before antitoxin is given. It still remains to be seen to what extent relaxants combined with adequate control of respiration, as in anaesthesia, can lower the mortality.—I am, etc.,

Cambridge. LESLIE COLE.

SIR,—It is obviously right that failures of a new form of treatment should be given as much prominence as are successes, and Dr. J. H. McIntyre (*Journal*, October 17, p. 866) does service in recording two fatal cases of tetanus in which muscle-relaxants were included in the treatment.

It has long been held that, when the incubation period is as short as a week, treatment of this disease is ineffective. I believe that the proper use of the muscle-relaxants may enable us to change our outlook, and I am sorry that Dr. McIntyre should support the fatalistic attitude on the experience of his two cases. These, as he says, do not make impressive reading, but I suggest that the potentialities of the muscle-relaxants were not exploited to the full. The exaggerated motor activity of tetanus can be treated either by drugs which act centrally—the narcotics; or by those which act peripherally—the muscle-relaxants. The narcotics all act on those parts of the central nervous system which are already being attacked by toxin and are therefore harmful. The enormous potential value of the muscle-relaxants lies in the fact that they can defeat spasm without lowering vitality. They are difficult to give properly, because the amount needed to counter spasm may be enough to paralyse breathing; and because the amount needed to achieve the best balance in any patient may vary widely from minute to minute. These two difficulties can be met by the provision of positive pressure assisted ventilation whenever the breathing muscles have to be paralysed and by the use of a muscle-relaxant whose intensity of action can be varied from minute to minute to meet the changing need. Succinylcholine is such a drug; curare, gallamine, and mephenesin are not.

The main cause of death from tetanus is usually respiratory infection but with anoxic episodes, exhaustion, and toxaemia as important contributory causes. This is because the tetanus toxin acts on the medullary nuclei, particularly on the nucleus of the vagus, so that the actions of the larynx and pharynx become disorganized. There is thus difficulty in swallowing, and spill-over from the pharynx into the tracheo-bronchial tree, with resulting respiratory infection. The best safeguard against this is early tracheotomy, and I believe this should be done in all cases of severe tetanus, not only because it lessens the likelihood of infection, but also because it prevents that constant irritation from bronchial secretions which accounts for much of the spasm.

If we adhere to the principles of early tracheotomy, assisted respiration, *continuously controlled relaxation*, and the restriction of central depressants—coupled, of course, with adequate doses of antitoxin—we may be able to save cases which would formerly have been regarded as hopeless. One patient was recently treated on these lines and she recovered.[1] Her illness was less severe than those described by Dr. McIntyre; but the methods used might bring some hope where previously there was none, and this letter is a plea for them to be tried.—I am, etc.,

Bristol. RONALD WOOLMER.

REFERENCE

[1] Woolmer, R. F., and Cates, J. E. (1952). *Lancet*, 2, 808.

Heartburn in Pregnancy

SIR,—In your annotation on heartburn in pregnancy (*Journal*, October 17, p. 873) you refer to nine cases of hiatus hernia in pregnancy described by Dutton and Bland and you state that "heartburn in pregnancy may therefore be of some importance."

We have tried for a long time to convince doctors that the subject is indeed of great importance, and in the *Lancet* we went so far as to say that we believed the key to the whole problem of incompetence at the cardia lay in the study of these cases.[1] At present we are reviewing 55 cases of hiatus herniation found in pregnancy two years ago.

We still consider that regurgitation and not herniation is the main factor in the production of symptoms. Further, it seems likely to us that this massive regurgitation of gastric contents, so common in pregnancy, may be a very important factor in the aetiology of early post-anaesthetic chest complications in pregnancy. It certainly produces nocturnal cough in many of these cases and it may be that with the abolition of the cough reflex under anaesthesia aspiration of the regurgitated fluid causes "spill" pneumonia. We are studying this subject, but because of the great frequency of heartburn in pregnancy and the difficulty, therefore, of obtaining figures of statistical significance the problem should be studied by many workers.

It would be a great help if someone would determine the true incidence of heartburn in pregnancy, paying strict attention to the definition of the term. With regard to the observation by Williams[2] that prostigmin is effective in treatment, we have injected prostigmin during the screening of patients but have failed to demonstrate any change in the appearance of the hernia or the volume or frequency of the reflux. We have not been able to relieve the symptoms by the use of prostigmin.—I am, etc.,

Bickley, Kent. N. D. MCCREATH.

REFERENCES

[1] Lawler, N. A., and McCreath, N. D. (1951). *Lancet*, 2, 369.
[2] *Amer. J. Obstet. Gynec.*, 1941, 42, 814.

Venepuncture in Young Children

SIR,—Dr. I. A. B. Cathie, in his article on venepuncture in the "Clinical Pathology in General Practice" series (*Journal*, October 24, p. 930), says, when writing about infants, "From birth to the age of about 3 years visible or palpable veins cannot be expected, and some other approach must be made." I must dissent from this view. I find that in the majority of cases veins are palpable in one or other antecubital fossa, even if not visible, and it is more often than not easy to get blood in quantity using the same technique as for adults, even in infants 24 hours old. I think it is so generally assumed that venepuncture at this site in infants is difficult that it is not even explored. A palpable vein here saves much time and trouble. I find that a needle and attached rubber tubing is easier to use for this purpose than a syringe. Needless to say, the vein is not visible nor palpable except with pressure from above. It is not necessary to see the vein, but it must be palpable, and usually is.—I am, etc.,

Canterbury. I. B. MORRIS.

SIR,—Dr. I. A. B. Cathie's advice to general practitioners on the withdrawal of blood from infants and young children (*Journal*, October 24, p. 930) is valuable technical instruction, and it is true that if a slick technique is acquired the whole procedure can be finished before the patient has had time to feel more than a little fear. On the other hand, as he admits, it does not always go easily, and surely the occasions when it is necessary to obtain blood from infants outside a children's ward must be so rare that the general practitioner can hardly hope to become expert unless he has had previous experience.

The venepuncture is thus quite likely to be unsuccessful at the first attempt, as it is even in a children's hospital. But Dr. Cathie has omitted any mention of possible harm from prolonging the procedure, for he says: "The traverse beneath the sternomastoid can then be repeated until the vein is entered," and, "If the attempt at venepuncture is unsuccessful on one side of the neck the same procedure should be carried out on the other," without giving any time limit. The actual pricks may not be very hurtful, but the child is too young to know that no more serious attack is to be made upon him. The fear engendered in the 2-year-old by immobilization in a blanket, the sight of the weapons, and the sometimes grim expression of the operator who wishes it was all over may cause lasting harm to a few children under certain circumstances. At the least, it makes the child afraid of doctors for a time, which is a disadvantage at the next consultation.

Venepuncture of infants and young children is necessary sometimes, and any harm it may do is usually trivial, but I should like to suggest that (*a*) it is done only when the doctor is quite certain that it is really necessary, (*b*) that the armamentarium is kept as much as possible out of sight, (*c*) that if it fails after a reasonable three-minute attempt it is abandoned for the day, and (*d*) that the doctor himself shows affection for the child afterwards in some way in order to counteract any impression that the thing is a punishment.

Dr. Cathie says towards the end of his paper that "failure to obtain blood can be the most exasperating and humiliating experience." He is referring to the person on the right end of the syringe.—I am, etc.,

London, S.E.1. D. G. VULLIAMY.

Cortisone and A.C.T.H.

SIR,—As a contribution to the discussion on the value or otherwise of these hormones in the treatment of rheumatoid arthritis, I give my experience of their use in 37 cases, treated in 1949 and 1950, and (apart from two patients aged 74 and 72 respectively, who died in 1951 of cerebral haemorrhage) examined or made contact with in 1953.

Careful selection of patients, to exclude pre- or co-existent tuberculous or focal infection, or poor psychological background, was exercised. All cases were treated in hospital, with the continuous co-operation of a physician colleague, the director of pathology, and the physiotherapy department. In these patients all the usual, and many of the unusual, forms of treatment had been employed, to the limits of polypharmacy, without material benefit. The hormones were supplied by relatives overseas, care being taken to ensure that, so far as possible, maintenance amounts should be available.

The results fall into three groups: (1) *Failures*.—Seven cases, where no response was obtained, or where alleviation was transitory, and not recovered even on larger doses of either hormone. (2) *Moderately Improved*.—Twenty-four cases, patients who have resumed their daily activities, in relative comfort and competence,

of whom eight were formerly bedridden or house-bound. The average maintenance dose is 75 mg. (three tablets) of cortisone, or, in a few cases, 10 units of A.C.T.H. per week. (3) *Complete Relief.*—Six cases; none of these patients has required a maintenance dose in the last two years; in three, no cortisone or A.C.T.H. has been called for in three years, and all live physically active lives.

Laboratory control is a necessary adjunct, especially with regard to the blood picture. It is useless to give either hormone where a significant degree of anaemia or reduction in cell volume exists; but neither the sedimentation rate nor the eosinophil count gives a constant guide to progress. Further, any alteration in the sodium/potassium balance is seen earlier clinically in loss of muscle tone than in the laboratory return. For these reasons daily observation of the patient in hospital is, in my view, essential.

Apart from the failures and the case noted below, side-effects have given no concern. Disturbance of water balance and oedema have been overcome by reduction of the fluid intake, by administration of 5 g. potassium chloride daily taken as table salt, and, if necessary, a brief intermission in administration; obesity, by control of diet; psychological aberrations, by care in selection of patients, eliminating the emotionally insecure.

Cortisone administration is essentially substitution therapy; A.C.T.H. stimulates the activity of the adrenal cortex and is effective only in so far as this has not atrophied and can respond. All six cases in group 3 had a four-day course, 20 units daily of A.C.T.H.; and I have the impression that its use is responsible for their "cure" and for the small maintenance dose of cortisone required in the patients in group 2. With the introduction of long-acting "acthar gel," a daily injection of 10 to 20 units makes treatment much easier, and it should, I believe, be tried.

Two cases call for special mention. One from group 1 had given a response to no therapy during seven years, including cortisone and A.C.T.H. His own doctor tried phenylbutazone ("butazolidin") with dramatic success, so that after five months the circumferential measurement of one knee had been reduced by 4 in. (10 cm.). The other, in group 3, had become acromegalic following a fractured base of skull 20 years previously, and was now the subject of active rheumatoid arthritis of polyarticular type, with massive effusion in both knees. The fact that she had formerly suffered from "nervous breakdown" was not forthcoming. After seven days' treatment by A.C.T.H., preferred on the theory that some degree of pituitary atrophy existed, she spent two nights writing poetry, which, believed by her to be original, was actually a reproduction of portions of the *Oxford Book of English Verse.* After an anxious 48 hours, the psyche returned to normal. Later, small doses of cortisone were substituted for A.C.T.H. and continued for four months, with much success. She has had no hormone—and no return of symptoms—since July, 1949, and has nearly full functional activity.

A number of patients included in this series (having read *The Times* extract (October 2) of the articles in the *Practitioner*[1 2]) have asked me to put forward this analysis. The joy of being able to get about and resume some degree of social and economic activity after being house-bound for considerable periods is something that the ordinary uninhibited individual has difficulty in appreciating fully. But I have no clue as to why the failure to respond was complete in the seven cases of group 1.—I am, etc.,

Sunderland. W. GRANT WAUGH.

REFERENCES

1 Dunlop, D. M. (1953). *Practitioner*, **171**, 343.
2 Tegner, W. (1953). Ibid., **171**, 424.

Treatment of Laryngeal Carcinoma by Radium Insertion

SIR,—I agree with Mr. W. Douglas Harmer (*Journal*, October 3, p. 735) that good results are obtained by radium insertion for laryngeal carcinoma, although I use a different method. In principle the technique is as follows.

The thyroid cartilage opposite to the lesion is drilled at its anterior end and three needles 1 cm. apart are inserted between the cartilage and parallel to the affected cord. Ellis[1] first described this technique for radon, and later I described it for radium,[2] adding a perspex stabilizer to ensure a parallel arrangement of the needles. The technique of loading a hollow needle-sheath can be altered to suit the size of the larynx and can deal effectively with lesions of the anterior commissure. It is likely that the physical distribution of dosage is more accurate and homogeneous than that employed by Harmer.

In a small series of cases treated from 1–4 years, all remain well with no evidence of cartilage necrosis. This technique is used in preference to external irradiation, and the amount of upset to the patient is about equal to that of Harmer's method.—I am, etc.,

London, W.1. ANTHONY GREEN.

REFERENCES

1 *Report of British Empire Cancer Campaign*, 1949, p. 142.
2 *J. Fac. Radiol. (Lond.)*, 1951, **2**, 206.

The Broken Acrylic Head

SIR,—I was interested in Mr. K. H. Pridie's letter (*Journal*, October 24, p. 939), as I have also been trying to overcome the faults that he mentions in the standard type of acrylic femoral head and have designed a prosthesis which appears to be rather similar to the one he illustrates. The usual pattern has a further disadvantage in that it transmits the weight to the narrow rim of the neck of the femur, which affords so small an area that bone absorption from excessive pressure must be expected, and indeed does occur.

The stem of the prosthesis shown consists of two flat plates joined together by a cross-member giving an H-shaped section which provides a maximum area for bone contact. The lower and inner plate lies on the calcar femorale, transmitting the weight directly to it along the normal lines of weight transmission, while the upper and outer plate affords counter-pressure against the outer cortex of the femur. The plate forming the base of the neck of the prosthesis also transmits weight to the upper cut surface of the calcar femorale. To reduce weight the rest of the neck and the interior of the hollow metal head is filled with resin. Thus the prosthesis is married to the femur along the normal lines of stress and transmits the weight over a large area. Moreover, being tapered, it will reseat itself if any bone absorption should occur. A possible disadvantage is that its point of junction with the femur is further away from the centre of movement and must therefore be subject to greater stress. Only time will show whether this factor outweighs other advantages of this type of prosthesis.—I am, etc.,

London, S.E.1. T. T. STAMM.

Mammary Abscess

SIR,—Following my recent plea (*Journal*, July 11, p. 98) for an investigation into the epidemiology of staphylococcal infections in maternity hospitals by means of bacteriophage typing, my attention has been drawn to the work of Dr. J. C. Colbeck,[1] who has done precisely this. His work appears to have attracted little attention in this country, although it was published in 1949, and its practical application is obvious.

Dr. Colbeck has shown that the infant may acquire in the nursery a pathogenic strain as early as 24 hours after birth or much later depending on its contacts. Undoubtedly the common source is another infant whose nasopharynx harbours the particular strain. Thereafter the feeding infant infects directly the mother's nipple. This explains perfectly

the apparent anomalies and provides the solution not only to mastitis in the mother but to staphylococcal ophthalmia and pemphigus in the infant. Its lesson is perhaps applicable to other problems such as neonatal dysentery. If for no other reason, hospital nurseries should be abolished and the infant should at all times remain in the same cubicle as the mother. In the interests of child psychology, etc., the principle of the child being with the mother is observed in some hospitals, but it is almost certain that the infants are collected together at times for certain purposes, which defeats the whole object so far as infection is concerned. May I commend Dr. Colbeck's paper to those administering our maternity hospitals?—I am, etc.,

Kirkcaldy. JAMES R. W. HAY.

REFERENCE

1 *Canad. med. Ass. J.*, 1949, **61**, 557.

Liver Biopsy

SIR,—Your annotation (*Journal*, October 17, p. 874) gave an admirable account of the present attitude towards liver biopsy, but one or two comments could be a little misleading. The mortality of liver biopsy is commonly supposed to be high (one frequently hears figures of 1–5% being used as arguments against using this investigation), and your reference to Davis,[1] who in 1946 discussed 4 deaths in 483 biopsies by various people, might foster this misconception. A more recent analysis of over 10,000 biopsies performed with modern techniques revealed a mortality of 0.12% and a significant morbidity of 0.32%.[2]

The statement that the abdominal route is "clearly safer in that the needle can more freely enter the liver" is possibly true, but one may add that with this route the needle can also more freely enter the gall-bladder, the stomach, and the colon. Most operators have now abandoned the dangerous subcostal route in favour of the intercostal approach except occasionally in gross hepatomegaly.

The description of biopsy material as 2–3 mm. in diameter would be unfortunate if it encouraged anyone to experiment with such large needles. I think you will find that needles with internal bores greater than 2.0 mm. are no longer used. The popular (but inefficient) Vim-Silverman needle has a bore of only 0.9 mm., although its outer needle is much larger. To use a bore greater than 2.0 mm. is to court disaster. Liver biopsy is rather more valuable in focal disorders of the liver than you suggest. In metastatic and granulomatous disease of the liver, an adequate specimen is diagnostic in 70–90%, depending on the technique employed. Provided a negative biopsy is not regarded as proof of normality of the whole liver, no error or confusion should arise. In addition to the value of liver biopsy in diagnosis, one may point out that it may be employed with great advantage and negligible risk in the management of a sarcoidosis, hepatic tuberculosis, chronic brucellosis, fatty metamorphosis of the liver, and the protracted case of viral hepatitis.—I am, etc.,

London, E.C.1. RICHARD TERRY.

REFERENCES

1 Davis, W. D., *et al.* (1946). *Amer. J. med. Sci.*, **212**, 449.
2 Terry, R. (1952). *British Medical Journal*, **1**, 1102.

Treatment of Malaria

SIR,—It has been suggested by Dr. R. Y. Taylor in a letter from Kenya (*Journal*, August 1, p. 285) that general practitioners in the Tropics could usefully make their records available to research workers and others. This almost echoes a similar request of mine.[1] I feel, therefore, that I should offer an account of nearly thirty years' experience of malaria treatment, in the hope that others also will contribute to help to clear up the confusion which undoubtedly exists and was referred to recently by my old friend Sir Philip Manson-Bahr (August 1, p. 284).

Thirty years ago there was one treatment for malaria: quinine, with its different salts—sulphate, hydrochloride, and hydrobromide. The last was thought to produce less tinnitus, but was seldom effective. Quinine remains the quickest drug to bring down temperature, but it is far from being the safest. Since the war not a single case of blackwater has shown up here, and this is probably owing to the fact that quinine is now used only in an emergency. During the Japanese occupation our fever hospital saw several cases of blackwater precipitated by alkaloids other than quinine. Just before the war three blackwater cases gave a history of having followed the use of "atebrin." On analysis, samples bought from the native shops where these tablets were said to come from were found to contain a yellow powder and 1½ gr. (0.1 g.) quinine. The maker's name overlapped the tablet, and both the size and colour differed from the original.

Almost everybody has now given up using quinine except in emergency, when it is given slowly by injection intramuscularly. Anyone who favours frequent quinine injections should try giving themselves one. I did it about 25 years ago as an emergency, and have not had one since: only a painful memory remains and a nodule. Quinine treatment in those days meant a course of 10 gr. (0.65 g.) thrice daily for one month, followed by 10 gr. twice daily for another month, and finishing with a daily dose of 10 gr. during the third month. It was normally given in capsule; the acid mixture frequently produced gastric irritation. An Italian patient preferred to drink bottles of quinine, iron, and arsenic, without any apparent ill effect. Several of the older planters spoke of taking as much as 90 gr. (6 g.) a day, and others took a drachm (4 g.) whenever they felt a rigor coming on. But most of these heroes knew nothing of bloodslides and parasites, and many died from blackwater.

If a patient relapsed on quinine sulphate, he was then given a course of the hydrochloride, or another quinine salt like quinidine sulphate. Intravenous N.A.B. was very effective for relapses. Pamaquin ("plasmoquine") came to our aid about the year I came to Malaya, and I remember being presented with a bill for extractions and a denture, said by my patient to be necessary as the result of pamaquin poisoning. This was soon followed by "quino-plasmoquine," one of the best pre-war treatments for relapsing malaria, but few of my patients could stand the full course of four or five tablets daily for a month, as originally recommended by the makers. A modified course, however, gave very satisfactory results in both vivax and falciparum malaria. Quartan is very rarely seen out here.

Then came mepacrine, originally called atebrin, and we used it with great care and in moderation, for it was known to produce yellowing of the skin, which, although not important, was not appreciated by the patients. But we soon found that in a few rare cases it produced mental excitement, sometimes requiring psychiatric treatment. Why it now can be used apparently harmlessly for such conditions as lambliasis in very much larger doses is difficult to appreciate. Malaria subjects who appeared to be unaffected by continuous quinine often did well on mepacrine, but it was disappointing as a prophylactic in small doses.

Then the Japanese invasion came, and all the progress in malaria relapsed to where it had been more than twenty years previously, and like those of most others my records, which included over 100,000 spleen palpations, disappeared into oblivion. But the war brought a big improvement in malaria treatment, and since then for some unknown reason, a subject of many medical discussions, malaria in Malaya has been no longer the very serious problem it used to be. Larvae surveys usually produce only few finds, whereas thirty years ago they were prolific.

Since the war mepacrine and proguanil have been used as a treatment for both vivax and falciparum infections. Three mepacrine tablets (100 mg. each) are given daily for three days, followed by three proguanil tablets daily for three days. To complete the course, I usually give a daily tablet of proguanil for one week. I cannot give any accurate relapse rate figures for this treatment, but am satisfied that it is not high.

Of the chloroquine products, I favour camoquin because it is easy to take (three tablets) and has a very low relapse rate. "Resochin" and "nivaquine" have given similar results, as one would expect from their similar formulae. Pyrimethamine ("daraprim") has proved rather disappointing. I do not wish to infer that the other chloroquines are not any good; they may be better. I mention those giving satisfaction out here, which I have used in my practice.—I am, etc.,

Johore Bahru, Malaya. NORMAN DUGDALE.

REFERENCE

1 *British Medical Journal*, 1948, **2**, 620.

Control of Tachycardia by Quinine

SIR,—Like Dr. P. R. Boucher (*Journal*, September 26, p. 727), I have had paroxysmal tachycardia from drinking coffee, but also, like Dr. H. L. Maclure (*Journal*, August 29, p. 511), I have successfully treated a case with quinine.

A woman of 77, who had had much malaria and dysentery in India but remained strong in body and spirit, came under my care three years ago with a history of frequent and severe bouts of paroxysmal tachycardia, sometimes lasting all day, for two years. Cardiologists had investigated her heart and found it normal. She had had "all sorts of *x*-rays." She stated that quinidine and digitalis were poison to her, and resented having been instructed, when these drugs failed, to take phenobarbitone and pull herself together. The patient stated that an attack was often preceded by a feeling of distension below the left costal margin. A barium meal showed a single diverticulum at the splenic flexure. Having seen the patient in a number of attacks, and confirmed that simple measures were ineffective and that various forms of digitalis by mouth, digoxin intravenously, and quinidine by mouth would all terminate an attack, but only by producing violent and alarming vomiting, I tried carbachol, and this usually terminated an attack, at the cost of tolerable diarrhoea instead of intolerable vomiting. Efforts were now made to prevent distension of the diverticulum by means of a low-residue diet, the regular administration of liquid paraffin and "taka-diastase," and courses of phthalylsulphathiazole. There was a reduction in the frequency of the attacks, but it was only when the patient took quinine hydrochloride 5 gr. (0.32 g.) three times a day that they became really infrequent, occurring at intervals of months instead of days. The lady is now 80 and her failing memory and pride cause her to prove the efficacy of these measures, because her attacks now occur when the medicines have not been taken for a few days.

I have not tried to terminate an attack by the injection of quinine bihydrochloride.[1]—I am, etc.,

Farnham Common, Bucks. DAVID MILWARD.

REFERENCE

1 White, Paul (1944). *Heart Disease*, 3rd ed. New York.

SIR,—The reaction of Dr. P. R. Boucher (*Journal*, September 26, p. 727) to Dr. H. L. Maclure's letter (*Journal*, August 29, p. 511) has stimulated me to draw the attention of your readers to the fact that quinine, not quinidine, was originally used in various abnormalities of the cardiac rhythm. In 1912 Wenckebach[1] discovered—more or less accidentally—the beneficial effect of quinine in some types of irregular action of the heart. His disciple Frey also studied this phenomenon, and he, together with Wenckebach, showed[2] that quinidine—the dextrorotatory isomer of quinine—acts almost twice as potently as does quinine. Since then quinidine has come to the fore in cardiology, but quinine is still used in some cardiac patients, often in combination with other drugs.

It is therefore quite possible that the paroxysmal tachycardia which Dr. Maclure describes in his patient was indeed controlled by the daily prophylactic use of quinine, but surely it is not necessary to assume that the use of proguanil was in one way or another connected with the patient's tachycardia, as Dr. Boucher has suggested.—I am, etc.,

Amsterdam. C. W. F. WINCKEL.

REFERENCES

1 *Die Unregelmässige Herztätigkeit*, 1914. Vienna.
2 *Berl. klin. Wschr.*, 1918, **55**, 450.

Histoplasmosis in Great Britain

SIR,—In a paper under this title, Dr. S. Locket and his colleagues (*Journal*, October 17, p. 857) reject as "very doubtful" a case of histoplasmosis from Africa, reported in England by me.[1] May I point out that this was a proved case of histoplasmosis, the diagnosis being based on the identification of the causative fungus in culture isolated from the lesion, and on the histopathology of the lesion.

This strain of *Histoplasma*, in its normal mycelial form, presented the specific morphological characters of *Histoplasma capsulatum*, but in the yeast phase, both in parasitic life and in culture, large forms developed which, although occasionally to be found in *H. capsulatum*, were much more marked and more constant in this tropical African strain. After prolonged study of the fungus in culture and in experimental disease I concluded that it could be distinguished from *H. capsulatum*, of which it was a stable variety, probably peculiar to tropical Africa. This opinion was borne out by the discovery and study of other cases of this form of histoplasmosis in various parts of tropical Africa. Recently Vanbreuseghem[2] accorded this variety specific rank under the name *Histoplasma duboisii*. The original strain isolated by me in 1943 is still available.

Including the case of histoplasmosis described by Locket and his colleagues, but not the one referred to at the conclusion of their paper, five well-authenticated cases of histoplasmosis have been identified in Great Britain since 1941. In all five cases there was a history of residence abroad in a warm climate; in three the disease was unquestionably contracted abroad; and in the other two there was no evidence that the infection was incurred in Great Britain. In fact the results of epidemiological surveys with the histoplasmin skin sensitivity test have failed to indicate the existence of endemic histoplasmosis in Great Britain.—I am, etc.,

Rickmansworth, Herts. J. T. DUNCAN.

REFERENCES

1 *Trans. roy. Soc. trop. Med. Hyg.*, 1947, **40**, 364.
2 *Ann. Soc. belge Méd. trop.*, 1952, **32**, 569.

A Human Blood-group Chimera

SIR,—I have read with the very greatest interest the report in the *Journal* of July 11 (p. 81) of a human blood-group chimera by Mr. I. Dunsford and others, together with your annotation (p. 89) on the subject. You mention a number of implications of this observation, but there is another to which I wish to draw attention.

It has been shown by Medawar and his colleagues[1] that skin homografts interchanged between non-identical twins in cattle may survive permanently, and I would venture to predict that if the twin of the blood-group chimera, reported by Dunsford, were still alive and skin homografts were made from one twin to the other these would probably survive permanently. It is clearly impossible to test this particular hypothesis, but it would be of great interest and importance to undertake reciprocal skin homografts if further blood-group chimeras are found. We are looking out for suitable cases here, but as the phenomenon is apparently a rare one I am writing to you in the hope that if the opportunity to perform an experiment of this kind arises elsewhere it should not be neglected.—I am, etc.,

Dunedin, N.Z. M. F. A. WOODRUFF.

REFERENCE

1 *Heredity*, 1952, **6**, 201.

A Danger of Succinylcholine Chloride

SIR,—At the close of an emergency operation performed at another hospital, under succinylcholine chloride ("scoline") drip with gas–oxygen anaesthesia, administered by one of us (J. W. M.) the drip was turned off by the anaesthetist but had not yet been disconnected when a surgical colleague restarted it, ignorant of the fact that the bottle contained 0.1% succinylcholine chloride.

In the hope of preventing an occurrence of this type of accident (which in the above case did not prove fatal) discussions with colleagues, the theatre sister, and the pharmacist have resulted in the adoption of the following safety precautions. The use, for succinylcholine chloride drip solutions, of transfusion bottles different in size and label from those normally used for ordinary intravenous saline therapy. Immediately the succinylcholine has been added to the bottle by the anaesthetist, a special stick-on "caution label" is applied to the bottle by him. This label is 3 in. by 2 in. (7.5 cm. by 5 cm.), red-edged, printed in bold red lettering on a white background, and worded as follows: "Caution. Succinylcholine muscle-relaxant has been added to this bottle."—We are, etc.,

J. W. MONRO.
W. K. SLACK.

London, E.11.

Heparin in Intravenous Infusion

SIR,—I would like to support Mr. H. F. Smith's suggestion (*Journal*, September 5, p. 569). I have followed a similar course for a number of years with advantage and without mishap. I have been in the habit of adding 0.5 ml. of the 1,000 units per ml. strength to each pint (0.57 l.), making 500 units per pint (0.57 l.). Run in at the usual rate of 40 to 60 drops per minute, or 0.57 l. in three to four hours, the clotting time was unaffected in 10 cases investigated. One got the impression that the life of drips, especially the more sticky ones of blood and glucose, was appreciably prolonged. To confirm this, heparin was added to alternate infusions required in a general surgical ward. Infusions which stopped before the fluid therapy was completed were compared in the two series, others being ignored. In a total of over 70 infusions the superiority of the heparin-treated fluids was not so marked as one had expected. Unfortunately, I have not the figures to hand, and in any case I understand they were of little significance statistically.

I would like to add a note of warning. I make a point of adding the heparin myself or entrusting it to a reliable assistant. At the same time a label is stuck on the bottle stating that 500 units of heparin has been added. This is to avoid further doses being added by people who know "he likes heparin in his drips."

I have seen a dose of 100,000 units of heparin—that is, ten times the standard dose—given intravenously, by mistake, at the end of an operation for ligation of the femoral vein because of recurrent emboli. There was no doubt about the massive haematoma that developed in the wound. However, after evacuation of the blood clot there was minimal bleeding and the wound healed well after secondary suture. No doubt as the haematoma increased in size the pressure on it increased, which tended to stop further bleeding; in any case, the action of heparin given intravenously only lasts for three to four hours, the clotting time of the blood then returning to normal. Though this set of circumstances may not hold in all cases, I feel that perhaps the dangers of bleeding after the use of heparin have been over-emphasized.—I am, etc.,

Nairobi. ANDREW HICKS.

Any Complaints?

SIR,—While endorsing wholeheartedly your leading article (*Journal*, August 29, p. 479) that medical students, and in particular those least likely to end up in general practice, should receive first-hand instruction in the conditions of it, may I protest against your suggestion that they should learn "what patients first complain of"? I believe that patients do not complain of their symptoms until we as a profession teach them to do so. They may complain of their neighbours' wireless, but they simply "have" a rash or a pain until we suggest the term complaint, with its innuendo of responsibility lying either with the doctor or more broadly with the Health Service and the community at large. Thus we sow the seed which may blossom as neurosis and bear the fruit of litigation.

Certainly our clear duty is to relieve our patient's symptoms, and, if possible, help him so to alter his external and internal milieu that his disease or injury may cure itself; but seldom shall we help him by accepting, or suggesting to him that we accept, the responsibility for it. Well equipped as we may be to kill micro-organisms and set fractures, a large part of our function is to help our patient to tolerate his dis-ease so long as it may last. "This is your pain"; "This is your skin's reaction to its environment"; "This I can offer to help your body to recover." "What have you come to see me about?" may be bad grammar (though not worse than, "What are you complaining of?"), but at least it is good medicine and can be followed by a discussion of symptoms as a matter of mutual interest and concern free from the emotional tone of plaintiff and defendant.—I am, etc.,

Bradfield, Berks. G. A. BECK.

Cancer and the Public

SIR,—I beg the favour of your pages to answer the multiple criticisms of my letter (*Journal*, October 3, p. 779).

Dr. Sidney Russ (*Journal*, October 17, p. 883) is not a "doctor" but a distinguished physicist, yet he exhibits a strange inconsistency when, as such, he insists on using wrongly the word "cure"—the obvious cancer may be surgically removed but the pabulum on which it grows remains, as do often the malignant cells which have been disseminated throughout the body. These by their growth may become manifest in a few weeks, a few months, or years, and we have no means of preventing it and often no means of detecting it until the end is near. He must know that some of these "5-year cures" merely continue with a disease a rather pitiable existence, at least as pitiable as those who have had no "cure" but continue to live for 7–10 years. All I ask to be told is the truth, not what is considered by some to be expedient, since it has but a temporary basis and permits and encourages a tremendous amount of useless expensive repetition. Dr. E. D. Y. Grasby (*Journal*, October 17, p. 883) can rest assured that I would quietly take all those measures which good medicine dictates, for I am at least as keen on a cure for cancer as any propaganda enthusiast is, but I believe that knowledge is so widespread that the patient is at least as safe for guidance in treatment in the hands of a sound practitioner, since he is not so obsessed or blinded by scientific aids on which the specialist solely relies.

Dr. Grasby states, "It is to allay such fears [of cancer] that education may be of service," but in a later paragraph to combat my statement that "the major manifestations of syphilis have been abolished even though secrecy and not propaganda has dominated treatment," he states: "Surely neurosyphilis may be completely incurable even with the most violent treatment." Most doctors would agree that if the public were told this it would hinder and not help to induce patients to come for treatment; though my statement, which is true, would. Propaganda for cancer has always increased the fear of it—it has led many healthy people to seek "check-ups"—but it will never induce the doctor who is a sufferer or a layman who has seen some of the results of treatment to divulge that which he knows is feeding "on the pith of life."

Let me reassure "A Grateful Patient" (p. 883) that I am fully alive, as are all general practitioners, to the benefits available from surgery where the cancer is occluding a vital tubular structure—the sooner a necessary plumber's job is done the better—and to comfort him further by telling him that I have a patient alive more than 20 years after resection of such a lesion of the colon. But that patient, like him, had complained of signs and symptoms which indicated the possible site of the lesion and she had the desirable surgery.

Are we to understand from Dr. John McFarland (*Journal*, October 24, p. 936) that the ignorance of the general practitioner was responsible for the patient's death? Let me comfort him and Sidney Russ with the words of a dying surgeon, Mr. Percy Furnivall[1]: "The surgical part of my case was trivial and painless. I would not wish my worst enemy the prolonged hell I have been through with radium neuritis and myalgia for over six months. . . . For an old man with an early growth to have an adequate surgical operation only would be well worth the possible extra risk of recurrence." and his obituary notice[2] ran: "He formed the opinion that the treatment he had undergone had increased his suffering and made his passing more difficult, and he wished in his love for humanity to save others from a like fate."

The personal experiences of William Gosse[3] are of a similar nature, and they still continue.—I am, etc.,

Birmingham, 15. JAMES F. BRAILSFORD.

REFERENCES

[1] *British Medical Journal*, 1938, 1, 450.
[2] Ibid., 1938, 1, 1076.
[3] Ibid., 1938, 1, 643.

Orthopaedic Care in Poliomyelitis

SIR,—It is always regrettable when senior members of our profession resort to bickering in public, and the present controversy between orthopaedic surgeons and Dr. Ritchie Russell is no more seemly a passage of arms than was to be expected. In the Leeds region for the past six years poliomyelitis has been treated by the combined and harmonious efforts of a consultant in infectious diseases, a neurologist, a research anaesthetist, and an orthopaedic surgeon in a team whose members have not yet had occasion to be jealous of each other's contribution. It would seem that a similar pattern of working in the treatment of poliomyelitis would be to the benefit of the country at large.—We are, etc.,

HUGH GARLAND.
JOHN M. P. CLARK.

Leeds.

POINTS FROM LETTERS

Sweating in Shock

Dr. J. S. H. WHITEHEAD (London, S.E.22) writes: The fact that sweating occurs under certain conditions in anaesthetized persons was said by your expert ("Any Questions?" *Journal*, August 29, p. 520) to be "teleologically unfortunate." Dr. Ronald Woolmer (*Journal*, October 10, p. 832) took exception to this on the ground that it was merely ignorance of the whole truth that made it appear so. Surely the term "teleologically unfortunate" is self-contradictory, for according to Webster's dictionary teleology is the theory that the phenomena of organic life are explicable only by purposeful causes.

The Couvade

Dr. THEODORE LOUCAIDES (Nicosia, Cyprus) writes: With reference to the correspondence published about the custom of the couvade (*Journal*, August 23, 1952, p. 454, September 6, 1952, p. 555, and September 20, 1952, p. 667), I suggest that the following may be the origin of the hitherto unexplained custom. According to Plutarch (*Theseus*, 20), Theseus on his way back to Athens from Crete was blown by the winds to Amathus (now Limassol, Cyprus), where he was obliged to leave Ariadne (the daughter of Minos) because she could not continue her voyage to Athens (she was pregnant and suffering excessively from seasickness). At Amathus Ariadne could not bear being abandoned by Theseus, and she fell into marasmus and died during labour. She was buried at Amathus in the forest of Ariadne-Aphrodite. When Theseus returned to Amathus to fetch Ariadne he was informed of the unhappy event, and before leaving Cyprus he erected two statues and inaugurated a feast in honour of Ariadne. He left money to the Amathusians so that they might celebrate the feast annually. As a result of this feast Ariadne came to be worshipped at Amathus as a goddess of midwifery, and women honoured her statues representing a woman holding a baby in her arms. The feast was held during Gorpieos month (latter half of August and first half of September), and during it a man lay down and cried and acted as a woman in labour.

Acute Inversion of the Uterus

Dr. B. BHATTACHARYA (Darlington) writes: I read with interest Dr. J. F. Enright's report of a case of acute inversion of the uterus (*Journal*, September 26, p. 714). I have made a study of this subject based on nine such cases, and I entirely agree with Dr. Enright that quick and gentle reposition of the inverted uterus is the secret of success. In my opinion this should be done as soon as possible after the occurrence.

Cancer and the Public

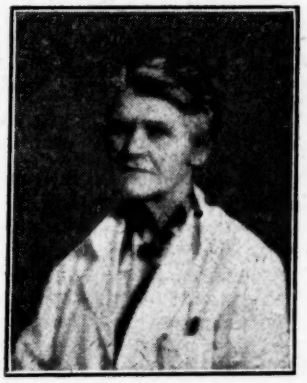
Mr. A. P. BERTWISTLE (Birmingham, 28) writes: With reference to Dr. J. F. Brailsford's letter (*Journal*, October 3, p. 779), I believe that cancer propaganda among laymen would do more good than harm if expressed in an optimistic vein, and this is justified by the results of surgery, aided by modern radiology, antibiotics, and anaesthetics. I think we have come to the stage when we can say that all skin cancers, and most lip, tongue, uterine body and neck, and rectum cancers if taken early are curable by surgery and radiotherapy. I understand early malignant disease of the lip is treated as an out-patient operation in the U.S.A. How can a doctor tell a patient that he or she should have come earlier, when they know nothing of early symptoms? There is considerable propaganda regarding venereal disease—*vide* the walls of public conveniences. Why should not cancer propaganda be more widespread in an effort to help humanity?

Obituary

E. CHRISTINE PILLMAN WILLIAMS, M.B.E., M.B., B.S.

Dr. Christine Pillman Williams died at her home in London on October 28 at the age of 64. She was the daughter of Mr. J. C. Pillman, a member of the Baltic Exchange, and was born on December 6, 1886, one of six children. Two of her brothers were famous players of Rugby football, and it was a special pleasure to Dr. Williams that her own four sons were all keen players.

Emma Christine Pillman went up to Girton College, Cambridge, in 1906, and took the natural sciences tripos in 1910. She qualified M.R.C.S., L.R.C.P. from the Royal Free Hospital in 1914, and obtained the London degrees of M.B., B.S. in 1916. After holding house appointments at the Royal Free Hospital until 1916, she worked at the Ministry of Munitions as chief medical officer at a shell-filling station; her war service there was recognized by the award of the M.B.E. in 1918. From 1919 to 1921 she was a member of the B.M.A.'s Ministry of Health Committee as the nominee of the Medical Women's Federation.



In 1919—the year in which she married Dr. Ulysses Williams, radiologist to the Royal Free Hospital—she returned to hospital to undertake research in the maternity wards with a Medical Research Council studentship. During her three-year tenure of this award she began, in collaboration with Dr. Lucy Wills, her work in the pathology department, which she continued on a voluntary basis until, in 1929, she was appointed lecturer in chemical pathology and chemical pathologist to the Royal Free Hospital. When war broke out again in 1939, the department of pathology was moved to the Three Counties Emergency Hospital at Arlesey, Bedfordshire, and Dr. Williams undertook full-time work there at the request of the Ministry of Health. She returned to London at the end of the war and took up her duties at the Royal Free Hospital again, being granted recognition as a teacher of the University of London in 1945, and appointed senior lecturer in charge of the department of chemical pathology in 1947. She was due to retire next year after 33 devoted years of work for her medical school and hospital. Her colleagues mourn her loss as a pathologist and as a very dear friend to many of them, and their sympathy goes out to her husband and family.

R. A. W. writes: Dr. Pillman Williams's long association with the Royal Free Hospital was temporarily interrupted on the outbreak of war in 1939, when the department of pathology was evacuated to Arlesey; she went with the first load of equipment and did not return to Gray's Inn Road until six years had passed. In the early months at Arlesey, when improvisation with makeshift apparatus was the rule, her cheerful acceptance of all difficulties and her help and encouragement in establishing teaching and hospital routine in the new and strange surroundings were invaluable.

Dr. Williams made a home for herself and her family on the outskirts of Letchworth, and there members of the staff and students were always sure of the warmest of welcomes. She was soon engaged in committee and subcommittee work, in addition to her routine and teaching duties, and her advice on dietary subjects was in demand from other hospitals near by as well as from her own. Dr. Williams gave unswerving loyalty to the Three Counties Emergency Hospital, as she had always done to the Royal Free, and as she was to do again in the years that followed 1945. Nothing could daunt her indomitable spirit. To see, as we did in the severe winters of 1940 and 1941, her Balaclava helmet bobbing above the great snowdrifts as she ploughed her way to work each morning was a sight to cheer the faint-hearted. The emergency hospital in the country owes to Dr. Williams, as it does to her clinical colleague, Mrs. Chodak Gregory, a deep debt of gratitude for their faithful service to all its interests.

In reorganizing the department of chemical pathology at the Royal Free Hospital after the war Dr. Williams worked unremittingly and did not spare herself, and she had the happiness of seeing it grow in stature and importance before her last illness took her from it. Her colleagues will miss her sorely. No one could have been kinder or more loyal. No one ever sought her help in vain.

D. C. H. writes: I first met Christine Pillman Williams in 1918, when she was in medical charge of the women in a munitions factory, which she invited me to visit with her. There she was tackling the problems of T.N.T. and allied poisonings and was winning the ready co-operation of all who worked under her by her sympathetic and understanding approach. A year or two later I was in daily contact with her at the Royal Free Hospital, where our association continued till 1937. Dr. Williams excelled as a clinical pathologist, and her help in the diagnosis of a difficult case was invaluable, for she viewed the problem as a whole and kept the clinical probabilities always in mind when advising on laboratory investigations. Anyone who had the privilege of working with her, whether as junior resident or one of the senior staff, owes her a debt of gratitude for the help she gave so readily from her funds of knowledge and experience.

Quite early in her career Dr. Williams became interested in the disorders of pregnancy and did valuable work on the biochemical changes associated with these disorders and with their dietetic treatment, and later we worked together on the dietetic treatment of rheumatoid arthritis. The effects of various diet treatments were studied from the clinical aspect with the concurrent biochemical changes, other therapeutic treatments being excluded. Some extremely interesting results were obtained and cinematograph records of clinical progress were made. The work, however, was interrupted by the outbreak of war in 1939. A modified form of Bircher-Benner diet was used in a number of cases, Dr. Williams being responsible not only for the drawing up of the diet sheets but for the close supervision of the preparation of the food in palatable form in the diet kitchen. Her biochemical research work covered many fields, but was always directed to clinical problems, to which she made many valuable contributions. Her loss will be mourned by all who knew and loved her.

N. S. FRASER, O.B.E., M.D.

The medical profession in Newfoundland has lost a prominent member by the death of Dr. N. S. Fraser at St. John's on October 6 in his ninetieth year.

Nutting Stuart Fraser was born in 1864, the youngest son of the late James Oliphant Fraser, one-time Member of the House of Assembly and a former Postmaster-General for Newfoundland, and grandson of the Rev. Donald Allan Fraser, pioneer kirk minister of the County of Picton, Nova Scotia. After receiving his early education at the Protestant Academy in St. John's he attended Queen's University at Kingston, Ontario, and matriculated with first-class honours in Latin and Greek. Later he entered Edinburgh University to study medicine, and graduated M.B., C.M. in 1886, in the same year passing the examination for the M.R.C.S. in London.

After graduation he held residential appointments at the Simpson Maternity Hospital and the Royal Sick Children's Hospital, Edinburgh, and then in 1887 returned to St. John's, Newfoundland, entering practice as a junior partner with the late Dr. Thomas Howley. From that time until his death he lived a life of devoted and unselfish service. In 1893 the Government of Newfoundland appointed him to the first medical board formed under the Medical Act, and he maintained his membership of the board for 60 years, being its president for the past 25 years.

In 1936 Dr. Fraser celebrated his fiftieth year in practice in a remarkable way. He wrote a thesis on some original studies, and was awarded his M.D. for this work by the University of Edinburgh. All through his professional career he kept his knowledge up to date, and as recently as September this year he took an active part in the discussions of the Newfoundland Medical Association and gave the members a short address on pancreatitis. He was a pioneer in many medical activities, including the use of *x* rays, and he established and maintained for many years the only children's hospital, as well as conducting a large general practice. He was a consultant on the staff of the general hospital, and for some years was port doctor and health officer for the port of St. John's. During the influenza epidemic of 1918 he was recalled to the health department, and by his strong action in closing all places of entertainment and banning mass meetings he did much to stop the spread of the infection. At the same time he organized a volunteer nursing service and temporary hospitals. In 1945 he was appointed O.B.E. for his medical work in St. John's.

Dr. Fraser was prominent in church circles and a faithful member of St. Andrew's Church as the senior elder and superintendent of the Sunday school. Numerous contributions on current topics and historical subjects were published over his initials in the local daily paper. He leaves four sons, one of whom, Dr. Nutting Stuart Fraser, is a consultant anaesthetist in Edinburgh, and another, Dr. J. Oliphant Fraser, is in general practice in St. John's.

Dr. C. E. MORRIS, a past president of the Chester and North Wales Medical Society, died at his home in Holywell, North Wales, on October 7, at the age of 81. A popular figure in the town since 1898, he had completed 50 years in practice before he retired a few years ago. Charles Edward Morris was born at Rhosllanerchrugog, near Wrexham, on May 31, 1872, and from Ruabon Grammar School he went on to study medicine at University College, Liverpool, and later at St. Mungo's College, Glasgow. He qualified in 1895 and then held a post as house-surgeon to Sir Robert Jones at the Royal Southern Hospital, Liverpool, an appointment which encouraged his keen interest in orthopaedic surgery. In 1898 he became resident surgeon at the Flintshire Dispensary, and after holding that appointment for some years he went into partnership with the late Dr. Owen Jones, of Holywell. During his professional life he was closely associated with the hospital at Holywell and often operated there. One of his main interests was obstetrics, and he was very accomplished in this work. He was surgeon to many of the industrial concerns in the area, and was often called to attend injured colliers at the coal-face. In the medico-political world he took a very prominent part. He

was secretary of the Denbigh and Flint Division of the B.M.A. from 1913 to 1917, chairman of the Division in 1924–5, president of the North Wales Branch in 1931–2, and he represented his constituency at ten Annual Representative Meetings between 1919 and 1935. He was also a former member of the Welsh Committee of the B.M.A. A member of the old Flintshire Insurance Committee for many years, he was also secretary of the local panel committee, and became a member of the Denbighshire and Flintshire Executive Council at its inception. In 1912 he saw the inauguration of the National Health Insurance scheme, of which he was a whole-hearted supporter, as he was of the National Health Service Act of 1948. His non-professional interests were many, and in particular he was a loyal member of his Church, serving on the representative body of the Church in Wales. A keen archaeologist, he was a member of the board of governors of the National Museum of Wales. At one time he was a member of the senate of University College, Bangor. Another of his interests was Freemasonry, in which he held several important offices. Dr. Morris will be greatly missed by his patients and colleagues; his kindly nature, his humility, and his versatility were only a few of his many virtues. He leaves a daughter and four sons, the eldest of whom, Dr. J. E. Ll. Morris, remains in practice at Holywell.—D. B. E.

Dr. S. B. HERD writes: When Dr. C. E. Morris, of Holywell, passed quietly on, there was extinguished a flame that had illumined with a bright steady light the medical, religious, and scientific life of Flintshire and regions further afield for many years. Charles Morris was not merely a fine general practitioner and no mean surgeon, as his long and devoted service to the Holywell Cottage Hospital showed, but a humanitarian in the very deepest and best sense of that word. He devoted his energies to the service of the people in the district, who loved him for his kindliness and sympathy, as well as they admired and trusted him for his skill. He was for many years an active member of the North of England Obstetrical and Gynaecological Society, travelling long distances to attend meetings, and was always held in respect and admiration. Many will remember how he would sometimes break his usual modest silence and enliven a discussion with the fruits of his long clinical experience. He found time, too, for archaeological and other non-medical interests, and his perennial energy even in his later years was the envy of his juniors. Behind his quizzical and habitually semi-humorous expression there was a tranquillity and steadfastness, a serenity and quiet confidence, on which he drew to meet the trials of bereavement and illness. To those around him he was able to pass on his serenity and faith.

Mr. ROBERT JAQUES, who died in Worthing Hospital on September 20 at the age of 91, was, before his retirement some 20 years ago, a consultant ophthalmic surgeon in Plymouth and a member of the honorary staff of the Royal Eye Infirmary. Born at Antrim, Northern Ireland, on February 28, 1862, he was educated privately and later became a medical student at King's College Hospital. He qualified in 1900 and obtained the diploma of F.R.C.S. three years later. After holding resident appointments at King's and at the Royal Eye Hospital, Southwark, he settled in practice at Plymouth as an ophthalmic surgeon. In his younger days Mr. Jaques took an active interest in medico-political affairs and was chairman of the Plymouth Division of the British Medical Association from 1911 to the end of the first world war and vice-chairman for four years thereafter. He was president of the South-western Branch of the Association in 1923–4 and a past president of the Plymouth Medical Society. A scholarly man with advanced political views, he foresaw much of the trend of medical practice as it is to-day. In 1909, for instance, he published a paper entitled "Nationalization of Medicine." Colleagues of his day will recall to mind his kind, whimsical disposition and his command of language as a public speaker. His death is regretted by many old friends in Plymouth.

We announce with much regret the sudden death on November 6 of Dr. JOSEPH BRAMHALL ELLISON at the age of 55. Educated at Rugby School, he saw service in the 1914–18 war in the Royal Engineers: he suffered severe shock as the result of being "buried alive" for several hours. Ellison went to Clare College, Cambridge, after the war, and thereafter to St. George's Hospital. He qualified M.R.C.S., L.R.C.P. in 1924, and took his Cambridge M.B., B.Ch. in 1925 and the M.D. in 1930, the same year in which he acquired the D.P.H. At St. George's, in the year of his qualification, he was awarded the Certificate of Honour and the Brackenbury Prize in Medicine. He was house-surgeon at St. George's and at Addenbrooke's and house-physician at the Queen's Hospital for Children. Not long after these appointments he entered the Fever Hospital Service of the Metropolitan Asylums Board, later taken over by the L.C.C. For the past twenty-five years he had worked at the same hospital—the Grove Hospital, Tooting—content to remain there in a relatively junior position. Ellison's friends and colleagues had little doubt of the brilliance of his mind and of his potentiality for achieving a more outstanding position in medicine than he did. His many gifts and a wide range of non-medical interests probably made it difficult for him to pursue with concentration any one course in life. He had a remarkable knowledge and appreciation of art, literature, and music, and he would take more pride in a poem he had written than in a paper published in one of the medical journals. At one time he embarked on the hazardous venture of promoting a film. Ellison was a stimulating and witty conversationalist, and no one could know him without feeling enriched by the experience. The guiding motive of his professional life was his unfailing affection for the sick children under his care in the fever wards of the Grove. He would prefer to spend his Christmas in the hospital so that he could entertain the children and make them laugh, and there must be in the neighbourhood of Tooting many hundreds of children who, with their parents, recall with deep affection his vivid and cheerful personality; they owe much to him. Ellison was a valued occasional contributor to the *B.M.J.*, and his knowledge of French and German was turned to good account in the work he did for *Abstracts of World Medicine*. His friends mourn the passing of a brilliant and lovable person whose character was marked with that eccentricity of personal idiom that is peculiarly English.

Universities and Colleges

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

At a meeting of the Council of the College held on July 25 the following officers were re-elected: *President*, Mr. Arthur A. Gemmell; *Vice-presidents*, Professor G. I. Strachan, Mr. A. J. McNair; *Honorary Treasurer*, Mr. A. C. H. Bell; *Honorary Secretary*, Mr. H. G. E. Arthure; *Honorary Librarian*, Mr. A. J. McNair; *Honorary Curator of the Museum*, Mr. A. W. Bourne; *Honorary Treasurer, Canadian Regional Council*, Mr. W. R. Foote. The following officers were elected: *Honorary Treasurer, Australian Regional Council*, Mr. J. N. Chesterman; *Honorary Treasurer, New Zealand Regional Council*, Mr. J. E. Giesen.

The Bernhard Baron Research Scholarship has been awarded to Mr. Stanley Albert Way for research on problems connected with the early diagnosis of cancer in women.

The following candidate was admitted to the Membership: D. S. Burris.

The following candidates were elected to the Membership: L. J. Abramowitz, S. Alankaram, W. J. R. Anderson, G. S. Andrew, A. K. Bose, J. C. Brace, E. R. Broadberry, T. J. Buckley, S. Burke, R. K. Burt, J. G. Cameron, R. S. Casement, Po Wong Christina Chow, Maureen D. Connolly, R. L. Edwards, M. B. Flanagan, F. M. C. Forster, Kathleen M. Frith, M. C. G. Grant, P. B. Guastalla, R. H. J. Hamlin, J. W. S. Harris, C. A. Jones, R. Ll. Jones, I. R. Macdonald, Betty Mallace, G. A. Manly, D. N. Menzies, M. C. Michelow, J. Nattrass, H. H. Neifeld, F. N. Neser, J. P. O'Dwyer, D. R. Patnaik, Clara Phillips, B. G. Pickles, W. Rotheram, J. S. Scott, J. M. Stewart, R. A. Struthers, Valerie M. Thompson, C. J. Thornberry, H. Ulman, C. G. Wilson.

Medical Notes in Parliament

SOCIAL SERVICE LEGISLATION IN NEW SESSION

The Queen's Speech opening the new session of Parliament on November 3, stating the Government's intentions to strengthen the national economy and thereby to safeguard the high standards of the social services, attracted diverse comment in the subsequent debates. The Speech also promised legislation to consolidate and extend the law on the safety, health, and welfare of miners and quarrymen, to provide benefit for certain further cases of disablement from industrial diseases, to amend and consolidate the law relating to food and drugs, and to restrict night working in the baking industry.

The EARL OF ROTHES, who moved the Address in the House of Lords in reply to the Queen's Speech, spoke as a governor of a London teaching hospital in expressing some disquiet about the rising cost of the Health Service. He said it had been thought that the high initial cost would tend to stabilize itself, because a better service would mean better health and a consequent reduction in demand. In practice the reverse seemed to be happening—both demand and cost had increased. It was unthinkable to try to stop the advance of medical science, so it would seem that the country must face a rising cost year by year.

Prevention of Tuberculosis

Miss EDITH PITT, an industrial welfare officer elected in July for the Edgbaston division of Birmingham, who seconded the address in the Commons, directed attention to the treatment and prevention of tuberculosis. The stage had been reached when there was an opportunity to eradicate it entirely. The number of ascertained cases awaiting hospital treatment remained the immediate problem. More beds were needed, more nurses, and improved surgical facilities. It would help to make the most effective use of existing beds if some kind of hostel or intermediate accommodation could be provided for those who only needed limited supervision and perhaps some nursing. A recent survey in the Midlands showed that between 15 and 20% of the beds occupied came within this group.

Mental Health

Mr. MALCOLM MCCORQUODALE hoped that the Royal Commission on the lunacy laws would consider closely whether there should not be a much greater separation between the problem of mental health and that of the mental defective. He would like to see mental hospitals, where the treatment was medical, and mentally ill patients remain under the Health Service; and colonies for defectives, whose treatment was a matter of care and education, returned to the local education authorities. He hoped also that the commission would not flinch from considering whether special medical treatment should be given to patients who had no control over their sexual appetites, and who were kept in institutions although in all other respects they could find a satisfactory place in society.

Mr. JAMES SIMMONS, who has worn an artificial limb since 1917, pleaded for some special consideration for the 24,000 men still surviving who had one or more limbs amputated in the first world war. They were an ageing group—the average age was 62—and they had special problems arising from the "wear and tear" from artificial limbs that should be compensated. A few years ago the Rock Carling committee was set up to inquire into the effect of amputation on the heart and lungs. Since that inquiry some limbless men—himself among them—had been personally examined. He hoped the Government would hasten the findings of the Rock Carling committee and announce their intentions for the limbless veterans.

"Smog" Masks and Research

Mr. SOMERVILLE HASTINGS asked the Minister of Health what research had been made to determine how much of the sulphur oxides and other gaseous contents of fog were removed from inspired air by the use of a dry gauze mask.

Mr. IAIN MACLEOD, replying on November 3, stated that there has been extensive research on protection from the toxic solid and gaseous contents of air in different conditions. Respirators to achieve this had been known for many years; they were of rather elaborate canister types, something like those used in the Forces. But the real problem of the "smog" was that of persons—and particularly old persons—suffering from weaknesses of the lungs or heart, as last winter showed, and further research was needed to determine what respirators could be safely worn by such people for long periods. This was going on actively among the out-patients of a large hospital. As to surgical gauze masks and chiffon scarves, he was advised that they would be of little or no value in absorbing the toxic gases, although, like any other comparable form of improvised protection, they would impede some of the solid particles.

EARL JOWITT in the House of Lords on November 4 urged the development of smokeless fuel and the extension of the smokeless zones.

LORD WOOLTON, replying for the Government, said an interim report was due soon from the committee appointed by the Minister of Fuel and Power.

Nerve Gases

Mr. IAN WINTERBOTTOM asked on November 9 if an antidote to nerve gases had been discovered, and referred to the recent death of a volunteer during experiments. Mr. DUNCAN SANDYS, Minister of Supply, replied that no complete antidote had yet been discovered. Mr. WINTERBOTTOM asked if the Minister could explain how the categorical statement that an antidote had been found had made its way into the American press by way of the *British Medical Journal* (August 9, 1952, p. 334, article from Chemical Defence Advisory Board). Mr. SANDYS replied that what he said was that no complete antidote had been found; a partial antidote had been found, but it was not regarded as wholly satisfactory.

Prospects for Registrars

The House of Commons had a short discussion on November 6 on the employment prospects of hospital registrars.

Mr. HORACE KING, who initiated it, recalled that in 1951, when it was discovered that there were more registrars than the Health Service could absorb, the decision was made to cut the intake of registrars to the approximate number of consultant posts likely to become vacant from year to year. His concern was with the men who already, in good faith, had taken posts as registrars and now found it difficult to obtain posts of any kind.

This problem confronted a group of 300 or 400 senior registrars. He described cases in the Southampton area to illustrate the difficulty the registrar had in trying to get into general practice: a surgeon-registrar who in desperation had taken a post in Australia; another registrar who did not even get on the short list for a vacant post in general practice; and a third who had hoped to become a consultant in general medicine but who had now switched over to pathology and taken a registrar's post.

He quoted also from a letter in the *Supplement* of October 3 (p. 161), "a bitter but revealing letter," he called it, "from a doctor who gave tragic pictures of the fate of three registrars," and from an annotation (*Journal*, p. 773), which said, "There is more than a grain of truth in the jocular remark . . . that to the applicant for a general-practice vacancy the possesssion of a car is more important than the possession of M.R.C.O.G., F.R.C.S., or—most dangerous encumbrance—M.R.C.P." It was a parlous state of affairs, Mr. King went on, when a medical journal could poke cynical fun at academic medical qualifications. It was bad for the health of the medical profession and of the Health Service. He did not blame the Minister. Vacancies were filled in the first place by a joint committee consisting of members of the health executive and the local medical committee; the former might be laymen, the latter were

entirely members of the medical profession. The short list went to the Medical Practices Committee, a national body consisting entirely of doctors, which finally made the appointment. So if a wrong was being done by the Health Service to registrars it was being done by members of the medical profession. The B.M.A. might be a very old trade union, but it was not as loyal to all its members as some others. The solution of the problem of registrars' entry lay largely in the hands of the profession, which dominated the committee which—independent of control—filled partnership and assistant posts as they became vacant. He urged that the Minister should use what influence he could by direct instruction, by exhortations to the medical practices committee and the local joint committees and to the B.M.A., and by direct action, if necessary, to see that the older registrars got a square deal.

Dr. BARNET STROSS said that many senior registrars found difficulty in obtaining consultant posts because of the reluctance of established consultants to allow them into the field at all. Since the emergence of the Health Service, and payment for all work, consultants' incomes had increased, sometimes in a spectacular fashion. But despite this there had been a decided reluctance by established consultants, particularly in the countryside, to allow any new men to come into this sphere of work.

Miss PAT HORNSBY-SMITH, Parliamentary Secretary to the Ministry of Health, said the fact that more men went into the senior registrar grade than it was possible to absorb into consultant posts in hospitals had been the subject of negotiations with the profession, and it had now been agreed that there should be an intake of approximately 270 new senior registrars each year. The number in the early years of training was now closely in line with this plan. But the number in the later stages of training was still in excess of the vacancies available. It was not the case, as Mr. King had said, that consultants were staying on longer.

The largest problem was in the category of registrars. It was never thought that all those who took registrar posts could possibly become specialists. The development of medical treatment and of the hospital service generally had called for many more registrars, and there was a grave shortage of this classification in some areas. This problem was under close examination by the profession and the Ministry, and it was clear that the remedies must include an increase in full-time and part-time registrars.

The main complaint of Mr. King was that there was discrimination against these registrars when they attempted to get into general practice. She thought too much emphasis had been put on the advertised vacancy relating to single-handed practices. It was not surprising that preference was often given in these cases to the man who had had general-practitioner experience. The wider field was unquestionably more in partnership than in advertised vacancies. There was far greater scope for a registrar to obtain an appointment in partnership, because it was unrealistic to think that the Medical Practices Committee, assessing the ability of a doctor to take over practice single-handed, and start in a new designated area, would overlook the doctor who already had general-practice experience. Generally speaking, a registrar had the highest qualifications in other ways, but his first steps in general practice would be far more advisably taken in a partnership. Having obtained that experience, he would, with his additional qualifications, be a very strong candidate for a single practice.

Dr. STROSS said he accepted this, but was any method available by which registrars looking for posts of this kind might know where they could apply?

Miss HORNSBY-SMITH replied that it was up to the partnerships to advertise, but she would examine the extent to which, by consultation with executive councils, they might know of vacancies that were imminent. She also pointed out that competition was particularly strong in the South of England, where there had been as many as 70 applications for single-practice vacancies. In the industrial North and in Wales there had been difficulty in getting one application for a designated area.

She disagreed with Mr. King's strictures on the medical profession. It had a dominating position on executive councils and on the Medical Practices Committee. One or two letters in the *British Medical Journal* had protested against the present method, but if it were reversed there would be enough letters to fill the entire journal from people who opposed the idea that anybody other than members of the profession were qualified to judge the suitability of those who wished to take up practice. In making their selections the Medical Practices Committee and the executive councils were doing a very good job.

Medico-Legal

VIOLINIST AWARDED DAMAGES

Damages of £1,240, with costs, were awarded by Mr. Justice Havers in the Queen's Bench Division last week to Miss Julie Saumarez, aged 43, of London, who sued the Medway and Gravesend Hospital Management Committee, alleging that negligent treatment of injuries to her left hand had ruined her career as a professional violinist.

Her case was that in a fall in July, 1949, she sustained a fracture of the base of the proximal phalanx of the left thumb and a chip fracture of the base of the distal phalanx of the middle finger of the left hand. On July 15, 1949, and on several occasions thereafter, until October, 1949, she attended the Sheppey General Hospital, Kent, for treatment, the doctor treating her being Dr. J. R. Theobalds. She was satisfactorily treated for the thumb fracture, but she alleged that Dr. Theobalds failed to discover or diagnose the chip fracture to the finger. Although she complained several times about the finger, and told him that an *x*-ray examination at the London Hospital had revealed a chip fracture, further examination was refused. As a result the bone had set in a crooked position, making it impossible for her to play the violin properly and thus ruining her career as a professional violinist.

The hospital management committee, denying negligence, contended that examination and treatment of Miss Saumarez's injured hand were properly carried out. They denied that she ever made any complaint about an injury to her finger. They did not admit that plaintiff had sustained any injury to her finger at all, and denied that she had suffered the damage alleged.

In evidence, Miss Saumarez said that when she first went to Sheppey General Hospital she did not know the nature of her injuries. Later she complained to Dr. Theobalds several times about pain in her middle finger. She said she told Dr. Theobalds she had been to the London Hospital and had been told that she had a chip fracture of the middle finger. He told her the *x*-ray plates at Sheppey showed no such injury.

Mr. R. Y. Paton, surgeon, called for the plaintiff, said that when he examined her in 1951 the distal phalanx of her left middle finger had a marked deviation. He considered the accident in 1949 was the most likely explanation of the deformity. The injury could have been remedied if discovered within three weeks.

Dr. Theobalds said in evidence that when the plaintiff first came to him a thorough clinical examination revealed injury to the thumb only. He had the thumb *x*-rayed, and treated it. On subsequent occasions he examined only the thumb specifically, but he would have noticed any obvious injury to the finger. On no occasion did Miss Saumarez complain about her finger or say anything about an *x*-ray examination at the London Hospital.

Called for the defence, Mr. O. J. Vaughan-Jackson, surgeon, said he examined plaintiff's hand in 1951 and found no injury to the middle finger, although there was a deflection of the distal phalanx. He was uncertain whether this had been caused by the accident or whether it was a pre-existing abnormality. Cross-examined, he agreed that the deflection should have been obvious on examination unless masked by swelling. He also agreed that either a deflection or a swelling ought to have been investigated further, although an *x*-ray examination might not have been necessary.

The Judgment

In his reserved judgment Mr. Justice Havers said it was not disputed that plaintiff now had a fairly obvious deflec-

tion of the distal phalanx of the left middle finger. The dispute was whether it was congenital or due to the accident. Another matter not disputed was that Miss Saumarez had her left hand *x*-rayed at the London Hospital on August 30, 1949. Here the dispute was why she went there, what the *x*-ray film showed, and whether she told Dr. Theobalds about it.

His lordship found that Miss Saumarez did suffer a chip fracture of the distal phalanx of the left middle finger in the fall in July, 1949, and that she complained about it to Dr. Theobalds. He accepted plaintiff's evidence that the reason why she went to the London Hospital for an *x*-ray examination was because she was worried about the condition of her finger.

He found that the injury was such that Dr. Theobalds should have discovered it on his first examination, or later. If he had discovered it, his duty would have been to make a further clinical and *x*-ray examination. It was even more incumbent upon him to make further inquiries if, as his lordship found, Miss Saumarez complained of injury to the finger. For these reasons his lordship held that Dr. Theobalds was lacking in that standard of care which he owed to a patient. The medical evidence was that, if properly treated, there was a good chance of such an injury being completely cured.

On the question of damages, the judge said he was driven to the conclusion that Miss Saumarez's career as a soloist or as a leader or deputy leader of an orchestra had come to an end before the accident. He thought the damage to her career as a result of the negligence of Dr. Theobalds was very slight. He assessed general damages at £900 and special damages at £340, and entered judgment, with costs, for the plaintiff for £1,240.

Vital Statistics

Week Ending October 31

The notifications of infectious diseases in England and Wales during the week included scarlet fever 1,226, whooping-cough 2,067, diphtheria 18, measles 842, dysentery 394, paratyphoid fever 8, and typhoid fever 4.

Poliomyelitis notifications (uncorrected) were as follows: paralytic, 88 (89); non-paralytic, 34 (46); total, 122 (135). This is a decrease of 13 compared with the previous week, the figures for which are in parentheses.

Infectious Diseases

Infectious diseases were more prevalent in England and Wales during the week ending October 24. Rises in the number of notifications included 207 for scarlet fever, from 1,062 to 1,269; 119 for measles, from 742 to 861; 94 for whooping-cough, from 2,096 to 2,190; and 78 for dysentery, from 232 to 310.

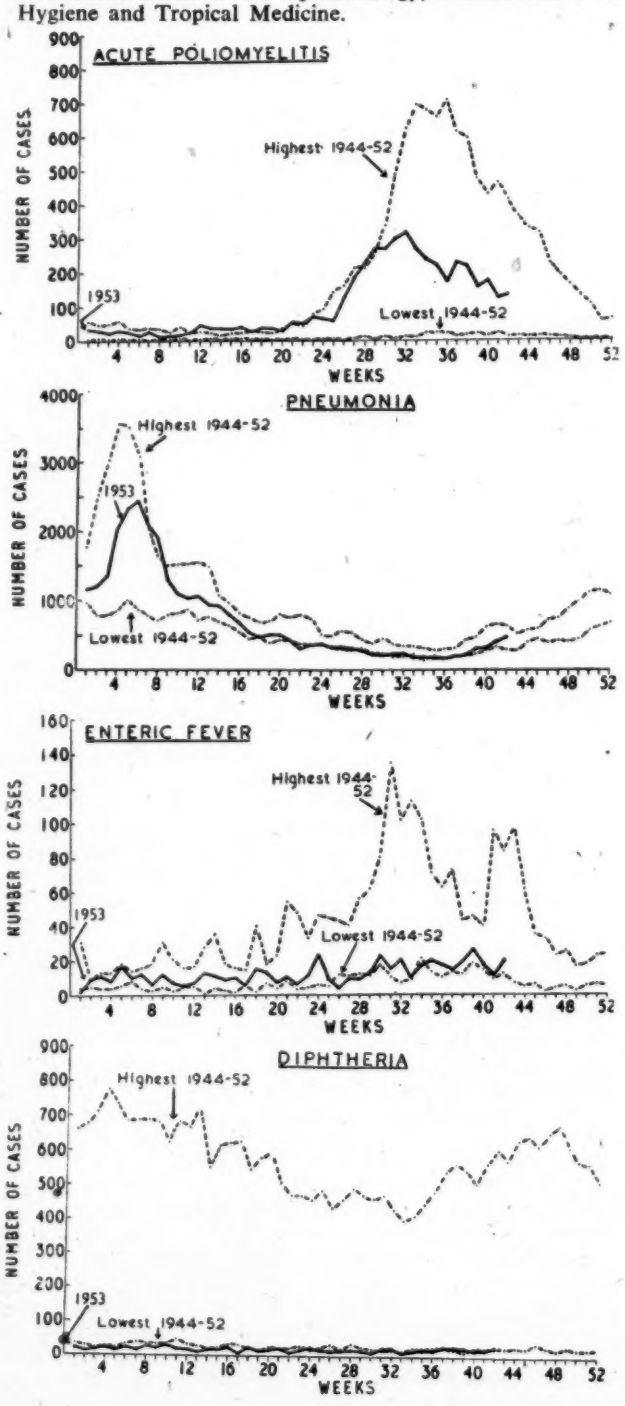
Only small rises were recorded in the local returns of scarlet fever; the largest was 35 in Yorkshire West Riding, from 155 to 190. The increase in the incidence of measles was due to the experience of the northern section of the country; in the southern section a small decrease was reported. The largest increase in measles was 67 in Lancashire, from 183 to 250. 29 cases of diphtheria were notified during the week, 9 more than in the preceding week. The largest rise was from 0 to 7 in Staffordshire. The chief centres of diphtheria were Lancashire, Liverpool C.B. 6; Staffordshire, Brownhills U.D. 4; Berkshire, Abingdon R.D. 3. Only small fluctuations were recorded in the local trends of whooping-cough. 9 of the 17 cases of paratyphoid fever were notified in Surrey, Merton and Morden U.D.

135 cases of acute poliomyelitis were notified during the week. These were 8 more for paralytic and 1 more for non-paralytic cases than in the preceding week. The largest returns were Yorkshire West Riding (Spenborough U.D. 3), Lancashire 13 (Liverpool C.B. 3, Preston C.B. 3), Nottinghamshire 10 (Nottingham C.B. 5), London 9, Warwickshire 9 (Birmingham C.B. 5), Southampton 7, Glamorganshire 7, and Kent 7 (Deal M.B. 4).

The chief centres of dysentery were London 66 (Islington 16, Chelsea 13), Yorkshire West Riding 40 (Bradford C.B. 14, Sheffield C.B. 11), Lancashire 37 (Royton U.D. 10), Yorkshire North Riding 28 (Middlesbrough C.B. 28), Kent 23 (Royal Tunbridge Wells M.B. 19), Gloucestershire 18 (Gloucester C.B. 9, Bristol C.B. 7), Northumberland 15 (Gosforth U.D. 6), and Middlesex 15 (Edmonton M.B. 7).

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1944–52 are shown thus - - - - - -, the figures for 1953 thus ————. Except for the curves showing notifications in 1953, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **October 24** (No. 42) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1953					1952				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire	Eire
Diphtheria	29	4	1	1	0	29	1	16	1	1
Dysentery	310	66	176	2	1	181	15	102	6	0
Encephalitis, acute	10	0	0	0		2	2	1	0	
Enteric fever:										
Typhoid	3	2	2	0	1	6	2	2	1	
Paratyphoid	17	0	1	0	1	15	0	1 (B)	0	
Food-poisoning	199	27		2		114	9		0	
Infective enteritis or diarrhoea under 2 years				25	32				13	20
Measles*	861	19	37	19	43	7,785	964	129	61	12
Meningococcal infection	34	1	14	0	2	30	0	12	1	1
Ophthalmia neonatorum	32	6	6	0	1	29	5	9	0	
Pneumonia†	475	31	146	9		439	23	224	1	
Poliomyelitis, acute:										
Paralytic	89	6	25	12	5	86	2	5	4	0
Non-paralytic	46	3				33	5			
Puerperal fever§	236	37	12	3	1	254	26	16	0	
Scarlet fever	1,269	81	237	30	69	1,760	171	331	26	61
Tuberculosis:										
Respiratory			157	30				135	21	
Non-respiratory			27	3				22	8	
Whooping-cough	2,190	130	251	43	34	1,074	63	111	35	33

DEATHS in Great Towns	1953					1952				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	1	0	0	0	0	1	0	1	0	0
Dysentery	0	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0		0	
Infective enteritis or diarrhoea under 2 years	7	1	0	1	1	7	0	1	0	1
Influenza	11	0	2	0	0	11	1	1	0	1
Measles		0	0	0	0		0		0	0
Meningococcal infection		1	2				1			
Pneumonia	180	32	28	8	6	173	25		16	7
Poliomyelitis, acute	4	0			0	2	0			0
Scarlet fever		0	0	0	0		0		0	0
Tuberculosis:										
Respiratory	117	13	11	2	11	104	9	19	4	6
Non-respiratory		0	2	0	2		5	1	0	3
Whooping-cough	1	1	2	0	0	1	0		0	0
Deaths 0–1 year	204	23	36	9	7	176	16	25	11	9
Deaths (excluding stillbirths)	5,000	745	555	86	154	4,951	702	556	133	169
LIVE BIRTHS	7,157	1047	857	205	382	7,323	1029	920	220	392
STILLBIRTHS	175	22	24			209	23	20		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

B.C.G. for School-leavers.—The Ministry of Health and the Department of Health for Scotland have written to tell local authorities that approval will be given to schemes for offering B.C.G. vaccination to children before they leave school. This is on the understanding that such schemes do not prejudice existing arrangements for the vaccination of tuberculosis contacts. Most children will be vaccinated in their 13th year, so that they can be followed up afterwards for a year at school. Children of 15 years and over are to be excluded so as not to interfere with the Medical Research Council's current trial of B.C.G. in school-leavers. The Ministry of Health states that there is as yet no scientific evidence of the true value of B.C.G. vaccination, and recognizes that some authorities may prefer to wait until the results of the M.R.C. trial are available in three years' time before themselves launching new vaccination schemes.

A New Journal.—*Radiation Research*, a journal devoted to all phases of radiation research, is to commence publication in February, 1954. Its object is to promote the integration of physics, chemistry, biology, and medical research, in so far as they are concerned with the effects of radiation on matter. The term "radiation" is interpreted broadly to include ionizing, ultra-violet, infra-red, and visible radiations. The journal will appear bi-monthly under the editorship of Dr. Titus C. Evans, University of Iowa, and be the official organ of the Radiation Research Society. The publishers are the Academic Press, 125, East 23rd Street, New York, 10.

Copley Medal.—Professor A. J. Kluyver, professor of microbiology at the Technical University, Delft, has been awarded the Copley medal of the Royal Society for his fundamental contributions to that science.

Nichols Fellowship.—The Council of the Royal Society of Medicine invites applications for a grant of £225 per annum for research in the fields of obstetrics and gynaecology. The award will be made for a period of one year in the first instance, but may be extended for a second year. Further details may be obtained from the Secretary, Royal Society of Medicine, 1, Wimpole Street, London, W.1. Applications must be received by May 15, 1954.

Leukaemia Award.—The Robert Roesler de Villiers Award was conferred on Dr. Ludwik Gross at the New York Academy of Medicine last month for his contributions to the knowledge of the nature and cause of leukaemia.

British Cardiac Society.—The autumn meeting of the British Cardiac Society was held in London on October 30 under the chairmanship of Sir John Parkinson. Both the morning and afternoon sessions were devoted to short communications arranged by Dr. Samuel Oram, the secretary of the society. They included papers on sodium chloride and cardiac muscle, pulmonary distensibility and respiratory work in mitral stenosis, cardiac output during exercise studied by the Fick method (illustrated by a film), pulmonary venous drainage into the right heart via a persistent left superior vena cava entering the left innominate vein, and the ballistogram in coronary artery disease. A dinner was held at Simpson's Restaurant.

Conference of Army Pathologists.—The 7th annual conference of Army pathologists was held at the Royal Army Medical College, Millbank, on October 22 and 23. The first morning was devoted to technical demonstrations arranged by the professor of pathology at the College, and in the afternoon there was an administrative meeting in the War Office. On the second day there were lectures by civilian guest lecturers. The annual dinner was held at the Junior United Services Club.

The Retiring Age at Oxford and Cambridge.—In congregation on November 3 the statutes of the University of Oxford were amended to permit employees of the University to remain in office until the age of 67. Previously the retiring age was 65. Similar legislation is under discussion by the Senate of the University of Cambridge.

Imperial Cancer Research Fund.—At a brief and pleasant ceremony on November 10 Professor H. R. Dean, chairman of the Imperial Cancer Research Fund's council, opened the Fund's new laboratories at 48, Lincoln's Inn Fields. This house is rented from the Royal College of Surgeons, and it has been converted inside into a modern laboratory building, with pathologists' rooms, biochemical and histological laboratories, and photographic department, all with up-to-date and labour-saving equipment. The research work will be concerned with outstanding problems of cancer in human pathology, and, as Professor Dean explained, efforts will be made to integrate experimental results with observations made on clinical material from the great London teaching hospitals. With the opening of the new laboratories the Fund now supports two separate research establishments: the Mill Hill laboratories, directed by Dr. James Craigie, F.R.S., and the Lincoln's Inn Fields laboratories, which will be supervised by Professor G. Hadfield.

Unicef Greetings Cards.—One way of supporting the work of the United Nations International Children's Emergency Fund is to buy the attractive greetings cards designed for the Fund by well-known artists. There is a choice of two sets: a Matisse design symbolizing the United Nations, and pictures by Lewitt-Him showing children at play in five areas of the world. Each card carries the season's greetings in the five official languages of the United Nations. Boxes of 10 cards, with envelopes, cost 7s. 6d., and orders should be sent to the Unicef Greeting Card Fund, 39, Kingsway, London, W.C.2.

COMING EVENTS

Harben Lectures, 1953.—Sir Henry Dale, O.M., F.R.S., will deliver the Harben Lectures for 1953 at the Royal Institute of Public Health and Hygiene, 28, Portland Place, London, W.1, on December 7, 8, and 9, at 5 p.m. each day. His subject will be "Changes and Prospects in Medicinal Treatment."

The Ferrier Lecture will be delivered on December 10 at 4.30 p.m. at the Royal Society by Sir Francis Walshe, F.R.S. He will speak on "The Contribution of Clinical Observation to Cerebral Physiology."

The 11th International Congress of Industrial Medicine will be held in Naples from September 13 to 19, 1954. Information about travel facilities may be obtained from Thomas Cook and Son, Ltd., Post Order Department (POD/L), Berkeley Street, London, W.1.

Fifth International Congress of Blood Transfusion.—The fifth International Congress of Blood Transfusion will take place in Paris from September 13 to 19, 1954, immediately following the International Congress of Haematology, which will be held from September 6 to 12, 1954. Further information can be obtained from Colonel (méd.) Julliard, 57, Boulevard d'Auteuil, Boulogne-sur-Seine, Seine, France.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Applications should be made first to the institution concerned.

Monday, November 16

HUNTERIAN SOCIETY.—At Apothecaries' Hall, 8.30 p.m., discussion: That Tobacco is a Blessing. Proposed by Sir Alan P. Herbert, M.P., and Dr. R. R. Bomford. Opposed by Sir Malcolm Hilbery, Q.C., and Dr. H. Joules.

●INSTITUTE OF CARDIOLOGY, National Heart Hospital.—9.30 a.m., Sir John Parkinson: Pain in the Chest.

INSTITUTE OF PSYCHIATRY.—5.30 p.m., Dr. E. Stengel: lecture-demonstration.

●POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Professor F. J. Nattrass: Difficulty in the Diagnosis of Epilepsy.

ROYAL EYE HOSPITAL.—5.30 p.m., Miss J. M. Dollar: Ophthalmic Nursing and Post-operative Treatment.

Tuesday, November 17

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor W. T. Astbury, F.R.S.: Some Recent Ideas about the Proteins and other Biological Macromolecules.

CHADWICK TRUST.—At Royal Sanitary Institute, 5.30 p.m., public lecture by Dr. John A. Logan, in collaboration with Dr. R. P. Burden: The Public Health Significance of Environmental Control by Engineering Means.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. E. J. Moynahan: Connective Tissue.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Theatre, 5 p.m., Professor R. J. Kellar: Recent Advances in the Study of Toxaemia.

SOCIETY OF APOTHECARIES OF LONDON.—4 p.m., Dr. P. M. F. Bishop: Disorders of Sex; 5.15 p.m., Dr. W. S. C. Copeman: Chronic Rheumatic Diseases: A Revaluation of Remedies.

SOUTH-WEST LONDON MEDICAL SOCIETY.—At Bolingbroke Hospital, Wandsworth Common, S.W., 8.30 p.m., Dr. James A. Robertson: Treatment of Diabetes.

WEST END HOSPITAL FOR NERVOUS DISEASES.—5.30 p.m., Dr. D. Gordon: Neuroradiological demonstration.

Wednesday, November 18

EUGENICS SOCIETY.—At Royal Society, 5.30 p.m., Mr. G. Aird Whyte and Dr. C. P. Blacker: Possible Future Activities of the Eugenics Society.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. O. Oliver: Bacteriology of Skin Diseases.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. D. I. Williams: Retention of Urine in Childhood.

MIDLAND MEDICAL SOCIETY.—At General Hospital, Birmingham, 8.15 p.m., clinical meeting.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Professor F. G. Young, F.R.S.: Some Aspects of the Endocrine Control of Carbohydrate Metabolism.

ROYAL EYE HOSPITAL.—5.30 p.m., Mr. J. F. P. Deller: Optics of Direct and Indirect Ophthalmoscopy.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW.—5 p.m., Dr. John Burns Lecture by Mr. J. J. Mason Brown: Surgical Treatment of Anomalies of the Alimentary Tract in the Newborn.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Dr. G. B. Mitchell-Heggs: Dermatology in Industry (illustrated).

Thursday, November 19

BRITISH INSTITUTE OF RADIOLOGY.—8 p.m., Dr. Sheila T. Callender and Dr. John Badenoch: Use of Radioactive Iron in the Investigation of Anaemia. Dr. E. H. Belcher, Ph.D., Mr. I. G. F. Gilbert, B.Sc., and Dr. L. F. Lamerton, M.Sc., Ph.D.: Experimental Studies with Radioactive Iron.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor G. W. Harris, F.R.S.: Stress and Thyroid Activity.

●CHARTERHOUSE RHEUMATISM CLINIC.—5 p.m., Gilbert Scott Memorial Lecture by Dr. J. F. Brailsford: Prevention, Detection, and Treatment of Osteo-arthritis.

EDINBURGH CLINICAL CLUB.—At 7, Drumsheugh Gardens, 8 p.m., Dr. J. G. Macleod: Chest Pain.

GLASGOW UNIVERSITY MEDICO-CHIRURGICAL SOCIETY.—At Glasgow University Union, 7.30 p.m., Mr. J. Hutchison: Abnormalities of the Oesophago-Gastric Junction.

HONYMAN GILLESPIE LECTURE.—At University New Buildings, Edinburgh, 5 p.m., Professor A. C. P. Campbell: Weil's Disease.

●INSTITUTE OF CHILD HEALTH AND INSTITUTE OF NEUROLOGY.—At National Hospital, Queen Square, W.C., 5.30 p.m., Dr. Macdonald Critchley: Speech Defects in Paralytic Syndromes.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5 p.m., Professor F. C. Ormerod: Malignant Disease of the Bronchus.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—11 a.m., Professor F. G. Young, F.R.S.: Some Aspects of the Endocrine Control of Carbohydrate Metabolism.

RESEARCH DEFENCE SOCIETY.—At Physiology Lecture Theatre, University College, London, 5.30 p.m., 22nd Stephen Paget Memorial Lecture by Sir James Learmonth: The Surgeon's Debt to Animal Experiments.

ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Sir Stanford Cade: Modern Conception of the Treatment of Cancer (with lantern slides).

ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Lloyd-Roberts Lecture by Dr. B. Ifor Evans: Science and Literature.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—3.45 p.m., Erasmus Wilson Demonstration by Dr. B. E. Heard: A Consideration of the Sites of Common Malignant Tumours.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At London School of Hygiene and Tropical Medicine, 7.30 p.m., laboratory meeting.

ROYAL STATISTICAL SOCIETY: STUDY CIRCLE ON MEDICAL STATISTICS.—At E.L.M.A. Lighting Service Bureau, 2, Savoy Hill, London, W.C., 6 p.m., Dr. Richard Doll: Smoking and Cancer of the Lung.

ST. ANDREWS UNIVERSITY.—At Physiology Department, Dundee, 5 p.m., Mr. J. F Riley: Physiological Function of Tissue Mast Cells.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. J. H. Paterson: neurology demonstration.

Friday, November 20

BRITISH INSTITUTE OF RADIOLOGY.—5 p.m., meeting of medical members.

FACULTY OF RADIOLOGISTS.—At Royal College of Surgeons of England, 4.15 p.m., "Carcinoma of the Ovary"—Dr. Walter Shanks: Survey of Cases Treated Between 1943 and 1950; Dr. C. L. Lewis: Use of Radioactive Colloidal Gold; Dr. Frank Ellis: Rationale and Results of Treatment of Carcinoma of the Ovary.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. E. J. Moynahan: Scleroderma and Allied Conditions.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—4.30 p.m., annual address by Professor Victor F. Lambert: Changing Pattern in Otology and Laryngology.

●POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. C. S. Hallpike: Vestibular Disorders.

APPOINTMENTS

BRISCOE-SMITH, J. H., M.B., Ch.B., D.P.H., Area Medical Officer, North-east Area of Warwickshire; Medical Officer of Health for the Borough of Nuneaton, the Urban District of Bedworth, and the Rural District of Atherstone.

CHEADLE ROYAL HOSPITAL, Cheadle, Cheshire.—William V. Wadsworth, M.B., Ch.B., M.R.C.P., D.P.M., Medical Superintendent; Alfred L. G. Smith, M.B., Ch.B., D.P.M., Deputy Medical Superintendent.

HAMILTON, JOSEPH STEWART, M.B., Ch.B., D.P.H., Medical Officer of Health and Principal School Medical Officer, City of Stoke-on-Trent.

MANCHESTER REGIONAL HOSPITAL BOARD.—D. E. Fletcher, M.B., Ch.B., F.F.R., D.M.R.D., Consultant Radiologist to the Barrow-in-Furness Hospitals; W. R. May, M.B., B.S., M.R.C.P., D.C.H., Consultant Chest Physician to the Rochdale and District Hospital Centre; J. R. Edge, M.D., M.R.C.P., Consultant Chest Physician to the Barrow-in-Furness Hospital Centre; Sheila A. Costello, M.B., Ch.B., D.A., Consultant Anaesthetist to the Bolton and District Hospital Centre; J. Ward, M.B., Ch.B., D.C.P., Assistant Pathologist to the Barrow-in-Furness Hospital Centre; R. Gibb, M.B., Ch.B., D.M.R.E., F.F.R., Consultant Radiotherapist, Christie Hospital, Manchester; Kathleen M. Rains, M.R.C.S., L.R.C.P., D.A., Consultant Anaesthetist to North Manchester Hospitals and Booth Hall Children's Hospital, Manchester; Marjorie A. Pollock, M.B., B.Ch., D.A., Consultant Anaesthetist to Royal Manchester Children's Hospital and Salford Royal Hospital; J. D. Blair, M.B., Ch.B., D.A., Consultant Anaesthetist to Lancaster and Kendal Hospitals; A. P. Buchan, M.B., Ch.B., D.P.H., Deputy Medical Superintendent and Assistant Psychiatrist, Brockhall Hospital, Langho, near Blackburn; H. E. Parry, M.B., B.S., M.R.C.P., D.C.H., Deputy Physician Superintendent, Monsall Hospital, Manchester.

MURRAY, DAVID S., M.B., Ch.B., F.R.C.S.Ed., Senior Orthopaedic Registrar, Dundee Royal Infirmary.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—E. G. W. Cross, M.R.C.S., L.R.C.P., D.P.M., and N. Lukianowicz, M.D., Assistant Physicians in Psychiatry at Bristol Mental Hospitals; J. N. Hoffman, M.B., B.S., Assistant Chest Physician to Bristol Clinical Area; Allan Hulme, M.B., B.Chir., F.R.C.S., Consultant Neurosurgeon to South-west Region in the Department of Neurosurgery at Frenchay Hospital, Bristol; J. M. Cuthill, M.B., Ch.B., D.P.M., Senior Registrar in Psychiatry at Tone Vale Hospital, near Taunton; C. P. Seager, M.B., B.Ch., and M. H. B. Joyce, M.B., Ch.B., Registrars in Psychiatry at Bristol Mental Hospitals; G. N. Arthurs, M.B., B.S., F.R.C.S., Senior Registrar in Neurosurgery, Frenchay Hospital, Bristol; J. M. Foreman, M.B., Ch.B., F.R.C.S.Ed., Surgical Registrar at Gloucestershire Royal Hospital, Gloucester; Jean E. Morgan, M.B., Ch.B., Registrar in Pathology to Bath Group of Hospitals; J. E. M. Dutton, M.B., B.S., F.R.C.S., Registrar in Neurosurgery, Frenchay Hospital, Bristol; John Harkness, M.D., Area Pathologist to South Somerset Clinical Area; E. J. T. Prettejohn, M.B., B.Chir., M.R.C.P., Consultant Dermatologist in South Somerset Clinical Area.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Bisset.—On November 4, 1953, at West Hartlepool, Co. Durham, to Dr. Sheona (formerly Lamont), wife of Dr. H. W. Bisset, a daughter—Christine Mary.

Copland.—On November 1, 1953, at Southmead Hospital, Bristol, to Dr. Elizabeth June (formerly Hunter), wife of Dr. William A. Copland, a daughter—Rosalind Susan.

Gray.—On October 31, 1953, at the Firs Maternity Hospital, Nottingham, to Elizabeth Katharine (formerly Mitchell), B.Sc., Ph.D., wife of Dr. William McWhinnie Gray, of Hucknall, Notts, a daughter—Katharine Ann.

Herdman.—On November 1, 1953, at Crickhowell Hospital, Brecon, to Betty Howarth, M.B., M.R.C.P., wife of Dr. G. J. S. Herdman, a daughter.

DEATHS

Bailey.—On October 11, 1953, at Collingwood, Davenport Park, Stockport, Cheshire, John Thomas Bailey, M.B., Ch.B.

Benett.—On October 14, 1953, at St. Helier, Jersey, Arthur Morris Benett, M.R.C.S., L.R.C.P., Lieutenant-Colonel, R.A.M.C., retired.

Brown.—On October 18, 1953, at his home, 63, Lauriston Road, London, E., James Jackson Brown, M.R.C.S., L.R.C.P., aged 71.

Chapman.—On October 16, 1953, John Ellis Chapman, M.R.C.S., L.R.C.P., of 6, Greenfield Avenue, Northampton, aged 79.

Falkner.—On October 21, 1953, at his home, Greenlands, Greystones, Co. Wicklow, Eire, Mervyn Winfred Falkner, F.R.C.S.I., Lieutenant-Colonel, R.A.M.C., retired.

Faulkner.—On October 18, 1953, in London, Cyril Douglas Faulkner, M.R.C.S., L.R.C.P., of Adelaide House, London, E.C., and 17, Clarence Gate Gardens, London, N.W., late of Stanford-le-Hope, Essex.

Fleming-Bernard.—On November 6, 1953, in a nursing home, Edinburgh, Andrew Milroy Fleming-Bernard, C.M.G., C.B.E., M.B., F.R.C.S.Ed., D.P.H., of Dunsinnan, Perth, late of Southern Rhodesia, aged 82.

Forrest.—On October 10, 1953, at his home, Glenmachan, Strandtown, Belfast, John Vincent Forrest, C.B., C.M.G., M.B., C.M., Colonel, A.M.S., retired, aged 80.

Gillett.—On November 3, 1953, in a nursing home, Oxford, Richenda Gillett, M.D., of 111, Banbury Road, Oxford, formerly of 5, Downshire Hill, Hampstead, London, N.W., aged 80.

Heathcote.—On October 14, 1953, Godfrey Heathcote, M.B., Ch.B., of 28, Wilmslow Road, Cheadle, Cheshire.

Hepworth.—On October 17, 1953, at Bedford House, Oakwood Lane, Roundhay, Leeds, George Hepworth, L.R.C.P.&S.Ed., L.R.F.P.S., formerly of Clarence Lodge, Morley, Leeds, Yorks, aged 83.

Hobbs.—On October 20, 1953, at The Sands, St. Mary's Bay, Ashford, Kent, Edward Coomber Hobbs, M.R.C.S., L.R.C.P.

Michell.—On October 13, 1953, Ralph Michell, M.R.C.S., L.R.C.P., D.P.H., of 10, Nugent Road, Southbourne, Hants.

Mitchell.—On October 10, 1953, George Fowler Mitchell, M.D., of Rugby, Warwicks.

Orchard.—On October 4, 1953, at The Hurst, Horam, Sussex, Wilfrid George Orchard, M.R.C.S., L.R.C.P.

Roberts.—On September 25, 1953, at the Military Hospital, Vancouver, Thomas Ernest Roberts, M.D., of Mayne Island, British Columbia, Canada.

White.—On October 7, 1953, at 31, Union Street, Oldham, Lancs, Adam Crawford White, M.D., aged 84.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Colonic Washouts

Q.—*Has the colonic washout any place in modern therapeutics? If so, when is it indicated and what are the benefits? Are there any special dangers?*

A.—The place of colonic washout in modern practice is not as limited as it probably should be. There is a distinct tendency for it to become a social habit, and it is not without danger if practised indiscriminately by inexperienced or irresponsible people. Haemorrhage from the trauma of the procedure and perforation of the bowel (especially of diverticula) have both been recorded more than once.

An irrigation is essentially a "washing" and should be so gentle as not to stimulate the defaecation mechanism. It may be used for cleansing the lower bowel preparatory to radiographic examination or surgery of the colon and rectum (for example, closing a colostomy); for assisting diagnosis—as before a sigmoidoscopic examination; and for introducing certain solutions whose object is either to increase or to relax the tone of the large bowel musculature.

Local pathological conditions of the anus or rectum, diverticulitis, and loose sphincter are contraindications.

Sulphur in the Air

Q.—*In what aerial concentrations are sulphur dioxide (SO_2) and hydrogen sulphide (H_2S) in the fumes from factory chimneys likely to cause (a) annoyance and (b) harm to the health of those living in the vicinity?*

A.—In urban air the concentration of SO_2 will usually be less than about 0.5 part per million (by volume), though in prolonged foggy weather it may be as high as 1.5 p.p.m. In flue gases from the burning of coal the concentration is likely to be 500 to 1,000 p.p.m. from the stacks of efficient industrial plant, and very much less from the domestic grate. Hydrogen sulphide is an uncommon industrial stack effluent except, perhaps, from gasworks, though even here most of the sulphide is absorbed in iron-oxide purifiers.

Sulphur dioxide is classified by Henderson and Haggard (*Noxious Gases*, New York, 1943) as a primary irritant which normally produces such violent irritation as to obscure any systemic toxic action, though La Belle has shown that soluble gases such as SO_2 have increased toxicity when carried into the lungs on an aerosol. At 3 p.p.m. the odour will be unpleasant, and throat irritation will be caused at 8–12 p.p.m.; 400–500 p.p.m. are dangerous for even short exposures, because suffocation may be caused by throat spasms. It is possible to become acclimatized to the gas, and 10 p.p.m. should be the maximum concentration for continuous exposure over a normal working day. Hamilton and Hardy (*Industrial Toxicology*, New York, 1949), however, write that chronic changes produced by SO_2 are more important than the acute irritation and quote Haggard as saying that there is no real tolerance to this gas and that the apparent tolerance is due to the production of a tenacious mucus from the chronic inflammation of the upper-air passages. Further, unpublished American work indicates that quite short exposures of healthy human subjects to concentrations not greater than 5 p.p.m. of SO_2 may result in a significant increase of pulse and respiration rate and in a reduction of tidal volume.

Henderson and Haggard also classify hydrogen sulphide as an irritant gas, especially at the low concentrations which may be expected to be produced by industrial effluents.

The gas may be detected by smell at about 3 p.p.m., but detection by odour should not be relied upon, as the olfactory nerve endings are readily paralysed by this gas. 20 p.p.m. should be regarded as the maximum allowable concentration for continuous exposure during the working day, to avoid conjunctival and other irritation. Exposures to 200–300 p.p.m. for up to four hours may produce nausea, belching, cough, headache, and dizziness, as well as irritation of the conjunctivae and blistering of the lips. Concentrations above 600 p.p.m. may produce death after upwards of 15 minutes' exposure and at 1,000 p.p.m. death may be instantaneous (Hamilton and Hardy). Henderson and Haggard write that moderately high concentrations may cause death from cessation of breathing owing to undue reduction of the CO_2 in the blood from overbreathing; very high concentrations cause respiratory paralysis. The hydrogen sulphide is rapidly oxidized in the blood, and once the symptoms of acute intoxication have passed off there should be no systemic sequelae.

Flat Foot

Q.—*(1) Is there a hereditary predisposition to flat foot? (2) At what age can the condition first be reliably diagnosed? (3) What prophylactic measures—for example, exercises or alteration to the shoes—are recommended for early cases, and at what age should they be begun?*

A.—(1) The evidence for a hereditary predisposition to flat foot is extremely vague. In general terms, it is probably not an inherited condition. However, it would seem likely that certain races are more predisposed than others.

(2) The ordinary child's foot appears flat because the arch is obscured by subcutaneous fat, and it is not until this disappears that an accurate diagnosis can be made. The time of this disappearance varies considerably in individuals, but certainly 18 months to 2 years may be regarded as the earliest age at which the diagnosis of flat foot can be accurately made.

(3) The wearing of good shoes, by which is meant shoes which are broad and well made, would seem to be the only prophylactic measure available. The part played by the muscles in the maintenance of the arch is disputed, but it seems unlikely that the performance of special exercises on a few occasions in a week can have much benefit, as the child is, in any case, actively using all these muscles all day long in his play. Not only is it doubtful whether these methods are of benefit as a prophylactic measure, but the use of exercises and wedges in the treatment of early cases is also of questionable value. The difficulty in flat foot is that there are no objective standards by which we may measure the severity of the condition, or improvement obtained by treatment, and at present a sceptical attitude to these measures is probably justified, but this is a matter of opinion, as there are few ascertained facts.

Clamping the Umbilical Cord

Q.—*For some time now I have refrained from clamping or ligating the maternal end of the umbilical cord on the grounds that this aids separation of the placenta. This practice was recently challenged. What is your expert's view? Of course, I ligate the maternal end of the cord when dealing with a multiple pregnancy.*

A.—This is an idea which most obstetricians have heard of from one of their earlier teachers, but it is rarely mentioned in modern textbooks. An exception is Stoeckel's *Lehrbuch der Geburtshilfe* (1930 and 1941 editions). In the past, however, it was a popular subject of dispute. In early times it was probably the general practice not to tie the maternal end of the cord, but during the seventeenth and eighteenth centuries certain European obstetricians advocated clamping it—some because they found that the turgid placenta after delivery was easier to demonstrate to students, some because they considered that the practice stimulated the uterus to expel the placenta more expeditiously. Smellie preferred to leave the cord untied, believing that its smaller bulk could pass more easily through the cervix, but he mentions the contrary arguments (vol. 1, p. 230, of the New Sydenham Society Edition of Smellie's *Treatise on the Theory and Practice of Midwifery*). The matter was never proved one way or the other and gradually ceased to attract interest, as it became clear that it had no practical importance. During more recent years a closely related subject which has received attention is the suggestion that overdistension of the placenta with saline injected through the cord (Mojon–Gabastou's method) facilitates separation and delivery of the "retained" placenta—again an idea which is not universally accepted.

In the routine management of labour the baby should not be separated from its mother until the cord has ceased pulsating, and in these circumstances the maternal end of the cord bleeds very little even if left untied. Moreover, by the time pulsation has ceased the placenta should already have separated. The conclusion, therefore, is that so far as the progress of the third stage is concerned it makes no difference whether the maternal end of the cord is tied or not. Clamping it merely prevents a little unnecessary soiling of the bed linen.

Ringworm of the Feet as an Industrial Injury

Q.—*Ringworm of the feet is fairly common among miners, particularly where pit-head baths are used. Should such cases be regarded as of industrial origin—for example, as a compensatable variety of dermatitis?*

A.—To obtain benefit under the Industrial Injuries Act an occupational dermatitis must be "produced by dust, liquid, or vapour." This designation is usually regarded as not covering infective conditions. In certain cases, however, where bathing after work is considered to be essential (for example, in coal-miners) infection from this fungus may be regarded as an "injury by accident" and benefit paid accordingly.

Trypsin Therapy

Q.—*What are the indications for trypsin therapy? How should it be given?*

A.—Trypsin therapy may be indicated when the pancreas has sustained severe damage as in chronic pancreatitis. In these circumstances it is possible that enteric-coated tablets of pancreatin (*B.P.*) may be beneficial. Recently trypsin has been given by inhalation in cases of bronchiectasis, as the enzyme is able to liquefy viscid secretions, but this application is still experimental and not without danger.

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